

FYI-07-01593

Document control Number 84070000083

is invalid. The submitter requested

that it be withdrawn and

replaced by FYI-07-01600,

Document control Number 84070000090.

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07/23/07



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FRAGRANCE MATERIALS ASSOCIATION OF THE UNITED STATES
1620 I Street, N.W., Suite 925
Washington, DC 20006
Telephone (202) 393-5800 • Facsimile (202) 463-8998
www.fmafragrance.org

Via Federal Express

August 16, 2007

CONTAIN NO CBI

TSCA Confidential Business Information Center (7407M)
EPA East - Room 6428 Attn: Section 8(e)
U.S. Environmental Protection Agency
1201 Constitution Avenue, N.W.
Washington, D.C. 20004-3302
(202)564-7672

RE: Submission of study results under Section 8(e) of the Toxic Substances Control Act (TSCA) for Oral Gavage Developmental Study with "dimyrcetol" 2,6-dimethyl-7-octen-2-ol (CAS Number 18479-58-8) and 2,6-dimethyl-7-octen-2-yl formate (CAS Number 25279-09-8) in Rats. Request to withdraw July 26, 2007 FYI Submission.

Dear TSCA 8(e) Coordinator:

On behalf of its members, the Fragrance Materials Association of the United States (FMA) is submitting test results from an oral gavage developmental study of "dimyrcetol" in rats, 2,6-dimethyl-7-octen-2-ol (CAS Number 18479-58-8) and 2,6-dimethyl-7-octen-2-yl formate (CAS Number 25279-09-8). The material that was tested in the developmental toxicity study in rats was a mixture of 44.2% 2,6-dimethyl-7-octen-2-ol and 54.8% 2,6-dimethyl-7-octen-2-yl formate.

I am requesting that the "FYI Submission" dated July 26, 2007 be withdrawn and replaced by this notification. In reporting the results of the study an inadvertent error was made in the identification of the substance that was tested. The July 26, 2007 submission only identified dimyrcetol (CAS No. 18479-58-8). This notice contains the correct information on the substance that was tested.

FMA is submitting information on this study pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA). This information was received through a draft final report from the contract laboratory that performed the study, Charles River Laboratories, Argus Division (Horsham, PA, USA). The study was conducted on behalf of the Research Institute for Fragrance Materials (RIFM). A draft final report of the study is enclosed with this letter. None of the member companies of the FMA have concluded that the results of this study indicate a potential substantial risk of injury to human health or the environment.

This study does not involve effects in humans. This notification does not contain confidential business information.



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Study Summary

The Research Institute for Fragrance Materials (RIFM) conducted the developmental toxicity study on "dimyrcetol," 2,6-dimethyl-7-octen-2-ol (CAS Number 18479-58-8) and 2,6-dimethyl-7-octen-2-yl formate (CAS Number 25279-09-8) and the draft report was recently received from Charles River Laboratories, Argus Division, where the study was conducted. Groups of presumed pregnant female SD rats were orally dosed (via gavage) with 0, 250, 500 or 1000 mg/kg/day dimyrcetol in a corn oil vehicle on days 7-17 of presumed gestation. On gestational day 21, all rats were euthanized, Caesarean-sectioned, and a gross necropsy was performed.

All rats survived until scheduled sacrifice. There were no adverse clinical signs that appeared to be test-article related. Body weight gains were reduced in the 1000 mg/kg group compared to the control group during the first few days of the dosage period but did not persist throughout the dosage or study period. Absolute and relative feed consumption values were significantly reduced in the 1000 mg/kg group compared to the control group on GDs 7-10, GDs 10-12, and for the entire dosage period. Despite feed consumption values that were comparable to the control group during the post-dosage period, feed consumption values remained significantly reduced for the entire gestation period.

Fetal weights in the 1000 mg/kg/day group were reduced approximately 3%, probably reflecting the maternal decreases in body weight and feed consumption that occurred during the first part of the dosage period. No other Caesarean-sectioning or litter parameters were affected by dosages of dimyrcetol as high as 1000 mg/kg/day. The 1000 mg/kg/day group had increases in the incidence of supernumerary thoracic ribs with associated significant increases and decreases in the numbers of thoracic and lumbar vertebrae, respectively. There was also a significant reduction in the average number of ossified hind limb metatarsals in the 1000 mg/kg/day group.

Due to the observed reduced maternal body weights and feed consumption during the dosage period in the 1000 mg/kg/day group, the maternal NOAEL was considered to be 500 mg/kg/day. The developmental NOAEL is 500 mg/kg/day due to the slightly reduced (3%) fetal weights and variations in skeletal ossification observed at 1000 mg/kg/day, a dose that also produced maternal toxicity.

These data will also be used to make a full risk assessment of the material under its present declared use and exposure as a fragrance ingredient.

Sincerely,



Glenn Roberts
Executive Director

Enclosure

From: Origin ID: BZSA (202)293-5800
John Cox
Law Offices of John H. Cox
1620 Eye Street, N.W.
Suite 925
Washington, DC 20006

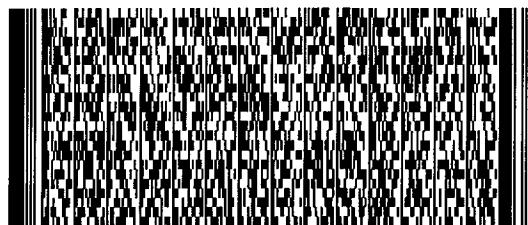


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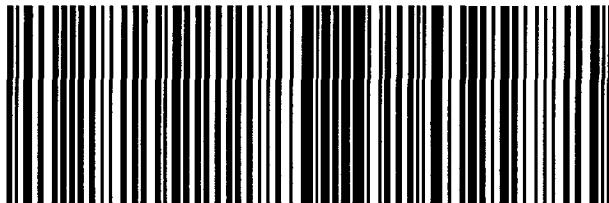
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DRAFT FINAL REPORT DATE: 9 MARCH 2006

ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL
IN RATS
PROTOCOL TIF00007

CHARLES RIVER LABORATORIES
PRECLINICAL SERVICES

DRAFT FINAL REPORT

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(PROTOCOL).

- a. Detailed descriptions of all procedures used in the conduct of this study are provided in the appropriate sections of this report and in APPENDIX C

All rats survived until scheduled sacrifice. There were no clinical observations that were considered related to dimyrcetol, and no gross lesions occurred. Body weights and body weight gains were reduced in the 1000 mg/kg/day dosage group during the first few days of the dosage period but these reductions did not persist throughout the dosage or study period.

All prepared formulations were acceptable for use on this study.

1.2. Results

All rats were sacrificed on DG 21, Cesarean-sectioned and a gross necropsy of the thoracic, abdominal and pelvic viscera was performed. Females were weighed and examined for sex, gross external, soft tissue and skeletal alterations. All rats were examined for sex, gross external, soft tissue and skeletal alterations.

Administration and once daily during the postdosage period. Body weights were recorded after dosage prematute deliveries and deaths before dosage, approximately three hours after dosage were recorded on DGs 0, 7, 10, 12, 15, 18 and 21.

All rats were examined for effects of the test article, abortions, each day.

One hundred pregnant CD-CD(SD) rats were randomly assigned to four dosage groups I through IV, 25 rats per group. The test article, Dimyrcetol, or the vehicle, corn oil, was administered orally (via gavage) once daily on days 7 through 17 of presumed gestation (DGs 7 through 17) at dosages of 0 (Vehicle), 250, 500 and 1000 mg/kg/day to rats in Groups I through IV, respectively. The dosage volume, 10 mL/kg, was adjusted daily on the basis of the individual body weight recorded before administration. The rats were administered once daily at approximately the same time each day.

1.1. Methods*

1. SUMMARY AND CONCLUSION

PROTOCOL NUMBER: TIF00007
PRECLINICAL SERVICES, PENNSYLVANIA
CHARLES RIVER LABORATORIES
TITLE: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

Absolute and relative feed consumption values were significantly reduced in the 1000 mg/kg/day dosage group on DGs 7 to 10, DGs 10 to 12 and for the entire dosage period, in comparison to the vehicle control group values. Values in the 250, 500 and 1000 mg/kg/day dosage groups were 107%, 102% and 87%, respectively, of the vehicle control group value on DGs 7 to 18. Despite feed postdosage period, absolute and relative feed consumption values remained significantly reduced for the entire gestation period, in comparison to the vehicle control group values.

Fetal weights in the 1000 mg/kg/day dosage group were reduced approximately 3%. Probably reflecting the maternal decreases in body weight and feed consumption that occurred during the first part of the dosage period. No other Caesarean-sectioning or litter parameters were affected by dosages of dimyrectol as high as 1000 mg/kg/day.

The 1000 mg/kg/day dosage group had increases in the incidence of supernumerary thoracic ribs with associated significant decreases in the numbers of thoracic and lumbar vertebrae, respectively. There was also a significant reduction in the average number of ossified hindlimb metatarsals in the 1000 mg/kg/day dosage group. No other gross external, soft tissue or skeletal fetal alterations (malformations or variations) were caused by dosages of dimyrectol as high as 1000 mg/kg/day.

On the basis of these data, the maternal no-observable-adverse-effect-level (NOAEL) of dimyrectol is 500 mg/kg/day. The 1000 mg/kg/day dosage of dimyrectol reduced maternal body weights and feed consumption during the dosage period, without adversely affecting the overall average maternal body weight.

The developmental NOAEL is 500 mg/kg/day. Fetal weights were slightly reduced (3%) and variations in skeletal ossification (increases in thoracic vertebrae and thoracic ribs and reductions in lumbar vertebrae and hindpaw metatarsals) were observed at 1000 mg/kg/day.

Alan M. Hoberman, Ph.D., DABT Date Director of Research

Ellise M. Lewis, Ph.D. Date Director of Reproductive Toxicology

Rebecca Gimildoro, M.S. Date Scientist and Study Director

1.3. Conclusion

property of the Sponsor.

The Sponsor owns the study. All raw data, analyses, reports and preserved tissues are the

2.1.7. Ownership of the Study

This study was conducted in compliance with Good Laboratory Practice (GLP) regulations of the FDA⁽²⁾, the Japanese Ministry of Health, Labor and Welfare (MHLW)⁽³⁾ and the Organization for Economic Co-operation and Development (OECD)⁽⁴⁾. Quality Assurance Unit findings derived from the inspections during the conduct of this study are documented and have been provided to the Study Director and the Testing Facility Management.

2.1.6. Regulatory Compliance

The requirements of the U.S. Food and Drug Administration (FDA)⁽¹⁾ were used as the basis for study design.

2.1.5. Study Design

The purpose of this study was to detect adverse effects of Dimyrcetol on CrI:CD(SD) presumed-pregnant female rats and development of the embryo and fetus consequent to exposure of the dam from implantation to closure of the hard palate. This study was designed to evaluate ICH Harmonised Tripartite Guideline stages C and D of the reproductive process.

2.1.4. Purpose of the Study

TIF00007

2.1.3. Study Number

Charles River Laboratories Preclinical Services, 905 Sheehy Drive, Building A,
Horsesham, PA 19044

2.1.2. Testing Facility

Research Institute for Fragrance Materials, Inc., 50 Tiec Boulevard, Woodcliff Lake,
NJ 07677

2.1.1. Sponsor

2.1. Conduct of Study

2. DESCRIPTION OF TEST PROCEDURES

2.1.8. Study Monitor

Valerie Turan Politan, Ph.D. (Human Health Scientist)

2.1.9. Study Director

Rebecca Cimilidoro, M.S. (Scientist)
Address as cited previously for Testing Facility.

2.1.10. Principal Scientist

Eliise M. Lewis, Ph.D. (Director of Reproductive Toxicology)
Address as cited previously for Testing Facility.

2.1.11. Technical Performance

2.1.11.1. Charles River Laboratories Preclinical Services

2.1.11.1.1. Pennsylvania

John F. Barrette, Sr., B.S. (Director of Operations)
Christopher A. Carboni, LATG (Manager Technical Operations)
Christine A. Tlak, B.S. (Study Supervisor)
Andrea M. Sweeney, B.S. (Laboratory Technician)
Julie A. Belzung, B.S. (Neurology Laboratory Technician)
Eunika L. Gray, B.S. (Formulation Laboratory Technician)

2.1.11.2. Massachusetts

Dorothy Savage, B.S. (Principal Investigator) - Concentration and homogeneity analyses

2.1.12. Subcontractor Facility

Dr. Anthony Leverone (Principal Investigator, IFF, Inc., Union Beach, NJ) - Bulk test article sampling

2.1.12. Report Preparation

Tsai-Liang Chiang, B.S. (Senior Report Administrator)
Tina M. Glemser, B.S. (Data Management Specialist)
Kellee M. Dello Russo (Study Coordinator)
Eliise M. Lewis, Ph.D.
Rebecca Cimilidoro, M.S.

a. DG is an abbreviation used for day of (presumed) gestation.

The test article was received on 30 August 2005 and stored at room temperature, protected from light.

2.2.3. Date Received and Storage Conditions

4103311

2.2.2. Lot Number

Dimyrectol - a clear liquid

2.2.1. Description

2.2. Test Article Information

The original report, raw data and reserve samples of the bulk test article and bulk vehicle are retained in the archives of the Testing Facility. Any preserved issues are retained in the archives of the Testing Facility for one year after the mailing of the draft final report, after which time the Sponsor will decide their final disposition. All unused test article formulations were discarded at the Testing Facility. Backup samples will be discarded at the Testing Facility following the issue of the final report. The bulk test article was discarded at the Testing Facility at the request of the Sponsor.

2.1.16. Records Maintained

DG 21 Caesaran-Sectioning

Dosage Period (DGs 7 through 17)

28 NOV 05 - 02 DEC 05

14 NOV 05 - 28 NOV 05

07 NOV 05 - 11 NOV 05

06 NOV 05 PM - 11 NOV 05 AM

01 NOV 05

DG^a 0

Cohabitation Period

01 NOV 05

Rat Arrival

06 NOV 05 PM - 11 NOV 05 AM

01 NOV 05

2.1.15. Dates of Technical Performance

4 November 2005

2.1.14. Date Protocol Signed

Alan M. Hobermann, Ph.D., DAIR (Director of Research)

2.1.13. Report Review

Documentation or certification of the identity, composition, strength, activity/purity and stability of the vehicle was provided by the Supplier to the Testing Facility. The vehicle is a marketed product and therefore the method of synthesis information has been documented. A Certificate of Analysis is available in APPENDIX D. The expiration date is January 2010.

2.3.5. Analysis of Purity

Standard safety precautions (use of protective clothing, gloves, dust-mist/HEPA-filtered mask, safety goggles or safety glasses with side shields) were taken when handling the vehicle.

2.3.4. Special Handling Instructions

The vehicle was received from Sigma-Aldrich Inc., St. Louis, MO, on 23 March 2005, 12 April 2005 and 13 and 19 September 2005 and stored at room temperature, protected from light.

2.3.3. Dates Received, Supplier and Storage Conditions

015K0115

2.3.2. Lot Number

Com Oil - a viscous yellow liquid

2.3.1. Description

2.3. Vehicle Information

Information to certify the identity, composition, strength, activity and/or stability of the test article was provided by the Sponsor to the Testing Facility. A Certificate of Analysis is available in APPENDIX D. The Sponsor's signature and approval of the protocol indicated that appropriate documentation of the method of synthesis, fabrication or derivation of the test article is on file and that it is available to the appropriate regulatory agencies should it be requested.

2.2.5. Analysis of Activity

Standard safety precautions (use of protective clothing, gloves, dust-mist/HEPA-filtered mask, safety goggles or safety glasses with side shields) were worn during formulation preparation and dosage administration.

2.2.4. Special Handling Instructions

Charles River Laboratories, Inc., Raleigh, NC

2.4.2. Supplier (Source)

Rate/Crit:CD(SD)

2.4.1. Species/Strain

2.4. Test System

APPENDIX E.

Information to document the stability of the prepared formulations bracketing the range of concentrations used in this study were provided by the Sponsor and are available in APPENDIX E. Results of homogeneity and concentration analyses are available in

of concentrations used in this study were provided by the Sponsor and are available in APPENDIX E. Results of homogeneity and concentration analyses are available in

2.3.8. Analytical Results

- a. A sample of the bulk test article was taken on the last day of treatment and shipped for analysis.
- b. IFF, Inc., Union Beach, NJ.
- c. Quadruplicate samples were taken from the top, middle and bottom of each concentration on the first day of preparation. Two samples from each quadruplicate set were shipped for analysis; the remaining samples were retained at the Testing Facility as backup samples. Two samples from each quadruplicate set were taken from each concentration on the last day of preparation. Two samples from each quadruplicate set were shipped for analysis; the remaining samples were retained at the Testing Facility as backup samples. Quadruplicate samples were taken from each concentration on the last day of preparation. Two samples from each quadruplicate set were shipped for analysis; the remaining samples were retained at the Testing Facility as backup samples. Quadruplicate samples were taken from each concentration on the last day of preparation. Two samples from each quadruplicate set were shipped for analysis; the remaining samples were retained at the Testing Facility as backup samples.
- d. Charles River Laboratories Preclinical Services Massachusetts, Worcester, MA.

Sample Type	Date Shipped To/Shipping Conditions	Storage Conditions	Date Received	Size	Date
Bulk Test Article ^a	IFF, Inc./Ambient conditions, protected from light	Room temperature, protected from light	28 NOV 05	5 mL	28 NOV 05
Bulk Test Article ^a	IFF, Inc./Ambient conditions, protected from light	Room temperature, protected from light	28 NOV 05	5 mL	28 NOV 05
Concentration and Homogeneity ^b (all levels)	CRL Preclinical Massachusetts, protected from light	Room temperature, protected from light	10 NOV 05	2 mL	24 NOV 05
Concentration and Homogeneity ^b (all levels)	CRL Preclinical Massachusetts, protected from light	Room temperature, protected from light	10 NOV 05	2 mL	24 NOV 05
Bulk Test Article ^c	IFF, Inc./Ambient conditions, protected from light	Room temperature, protected from light	28 NOV 05	5 mL	28 NOV 05
Bulk Test Article ^c	IFF, Inc./Ambient conditions, protected from light	Room temperature, protected from light	28 NOV 05	5 mL	30 NOV 05
Vehicle Reserve	Testinge Facility Archives	Room temperature, protected from light	05 JAN 06	5 mL	30 NOV 05
Vehicle Reserve	Testinge Facility Archives	Room temperature, protected from light	05 JAN 06	5 mL	30 NOV 05

2.3.7. Sample Information

Suspensions of the test article were prepared weekly at the Testing Facility. Prepared formulations were stored at room temperature, protected from light.

2.3.6. Test Article Preparation and Storage Conditions

USDA Registration No. 14-R-0144 under the Animal Welfare Act, 7 U.S.C. 2131 et seq.

2.5.1. Research Facility Registration

2.5. Husbandry

Male rats were given unique permanent identification numbers upon assignment to the Testing Facility's breeder male rat population. Breeder rats were permanently identified using a tail tattoo (ALMS Black Pigment #242, ALMS, Inc., Piscataway, NJ). Female rats were assigned temporary numbers at receipt and given unique permanent identification using Model® self-piercing ear tags (No. M5PT 20101, Gey Band and Tag Co., Inc., Morrisown, PA). Cage tags were marked with the study number, permanent rat number, sex, generation, test article identification, group number and dosage level.

2.4.7. System of Identification

Upon arrival, rats were assigned to individual housing on the basis of computer-generated randomization units. Healthy, mated female rats were assigned to four dosage groups (Groups I through IV), 25 rats per group, using a computer-generated (weight-ordered) randomization procedure based on body weights recorded on DG 0.

2.4.6. Method of Randomization

Number of Rats	130	01 SEP 05	Approximate Date of Birth	62 days	Age at Arrival	192 - 230	Weight (g) Day after Arrival	218 - 244	Weight (g) at Study Assignment
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2.4.5. Test System Data

The CD:CD(SD) rat was selected as the Test System because: 1) it is one mammalian species accepted and widely used throughout industry for nonclinical studies of developmental toxicity (embryo-fetal toxicity/teratogenicity); 2) this strain has been demonstrated to be sensitive to developmental toxicants; 3) historical data and experience exist at the Testing Facility (5-7).

2.4.4. Rationale for Test System

Female (Note: Male rats were used only for the purposes of breeding and are not considered part of the Test System.)

2.4.3. Sex

a.

See APPENDIX F (TEMPERATURE AND RELATIVE HUMIDITY REPORT).

study.

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the feed that would have interfered with the results of this study.

Analyses were routinely performed by the feed supplier. No contaminants at levels exceeding the maximum concentration limits for certified feed or deviations from expected nutritional requirements were detected by these analyses. Copies of the results of the feed analyses are available in the raw data.

2.5.7. Diet Analyses

Rats were given *ad libitum* access to Certified Rodent Diet® #5002 (PMI® Nutrition International, St. Louis, MO) in individual feeders.

2.5.6. Diet

Cage pan liners were changed at least three times weekly. Cages were cleaned approximately every other week.

2.5.5. Sanitization

An automatically controlled 12-hours light:12-hours dark fluorescent light cycle was maintained. Each dark period began at 1900 hours.

2.5.4. Light

Rats were individually housed in stainless steel, wire-bottomed cages, except during cohabitation period. During cohabitation, each pair of male and female rats was housed in the male rat's cage. All cage sizes and housing conditions were in compliance with the *Guide for the Care and Use of Laboratory Animals*⁽⁸⁾.

2.5.3. Housing

The study rooms were maintained under conditions of positive airflow relative to a hallway and independently supplied with a minimum of ten changes per hour of 100% fresh air that had been passed through 99.97% HEPA filters. Room temperature and humidity were monitored constantly throughout the study. Room temperature was targeted at 64°F to 79°F (18°C to 26°C); relative humidity was targeted at 30% to 70%.

2.5.2. Study Rooms

Rats were administered the test article and/or the vehicle once daily on DGS 7 through 17. The dosage volume was adjusted daily on the basis of the individual body weights recorded before dosage administration. The rats were administered the test article and/or route, the exact dosage can be accurately administered.

2.6.4. Frequency of Administration

The oral (gavage) route was selected for use because in comparison with the dietary route, the exact dosage can be accurately administered.

2.6.3. Route and Rationale for Route of Administration

Dosages were chosen based upon results from the dosage-range study TIF00006 with the same test article, Dimyrectol; 1000mg/kg/day has been selected as the high dose for this definitive study.

2.6.2. Rationale for Dosage Selection

a. The test article was considered 100% active/pure for the purpose of dosage calculations.

Dosage Group	Dosage ^a (mg/kg/day)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Number of Rats	Assigned Rat Numbers
IV	1000	100	10	25	11476 - 11500
III	500	50	10	25	11451 - 11475
II	250	25	10	25	11426 - 11450
I	0 (Vehicle)	0	10	25	11401 - 11425

2.6.1. Dosage Administration

2.6. Methods

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the water that would have interfered with the results of this study.

The processed water is analyzed twice annually for possible chemical contamination (Lancaster Laboratories, Lancaster, PA) and monthly for possible bacterial contamination (QC Laboratories, Southhampton, PA). Copies of the results of the water analyses are available in the raw data.

2.5.9. Water Analysis

Local water that had been processed by passage through a reverse osmosis membrane (R.O. water) was available to the rats ad libitum from an automatic watering access system and/or individual water bottles attached to the cages. Chlorine was added to the processed water as a bacteriostat.

2.5.8. Water

tissues for any possible histopathological evaluations of gross lesions.
tissues examined at necropsy were retained, in order to provide comparative
a. A table of random units was used to select one control group rat from which all

dead (there were no dead fetuses). Dead fetuses and late resorptions were differentiated
term fetuses that responded to stimuli. Nonresponding term fetuses were considered to be
which the occurrence of anomalies was grossly evident. A live fetus was defined as a
which organogenesis was not grossly evident. A late resorption was defined as one in
and late resorptions and live and dead fetuses. An early resorption was defined as one in
excised and examined for pregnancy, number and distribution of implantation sites, early
The numbers of corpora lutea were recorded. The uterus of each rat was

discarded when authorized by the Study Director.
apparently nonpregnant rats were retained in neutral buffer 10% formalin and were
between glass plates to confirm the absence of implantation sites. Uteri and ovaries of
was performed. Uteri of apparently nonpregnant rats were examined while being processed
Caesarean-sectioned and a gross necropsy of the thoracic, abdominal and pelvic viscera
All female rats were sacrificed by carbon dioxide asphyxiation on DG 21.

Skeletal alterations are available in the raw data.
Representative photographs of maternal gross lesions and fetal gross, soft tissue and
evaluation. Unless specifically cited below, all other tissues were discarded.
Gross lesions were retained in neutral buffer 10% formalin for possible future

2.6.6. Gross Necropsy^a

Body weights were recorded weekly during the acclimation period, on DG 0 and daily
during the dosage and postdosage periods. Feed consumption values were recorded on
DGs 0, 7, 10, 12, 15, 18 and 21.
The rats were also examined for clinical observations, abortions, premature deliveries and
observations and general appearance weekly during the acclimation period and on DG 0.
Rats were observed for viability at least twice each day for clinical
details before and approximately three hours after dosage administration, and once daily
during the postdosage period.

After acclimation, 130 virgin female rats were placed into cohabitation with 130 breeder
males rats, one male rat per female rat. The cohabitation period consisted of a maximum
of five days. Female rats with spermatozoa observed in a smear of the vaginal contents
and/or a copulatory plug observed *in situ* were considered to be DG 0 and assigned to
individual housing.

Vehicle once daily at approximately the same time each day. Prepared formulations were
stirred continuously during dosage administration.

2.6.5. Method of Study Performance

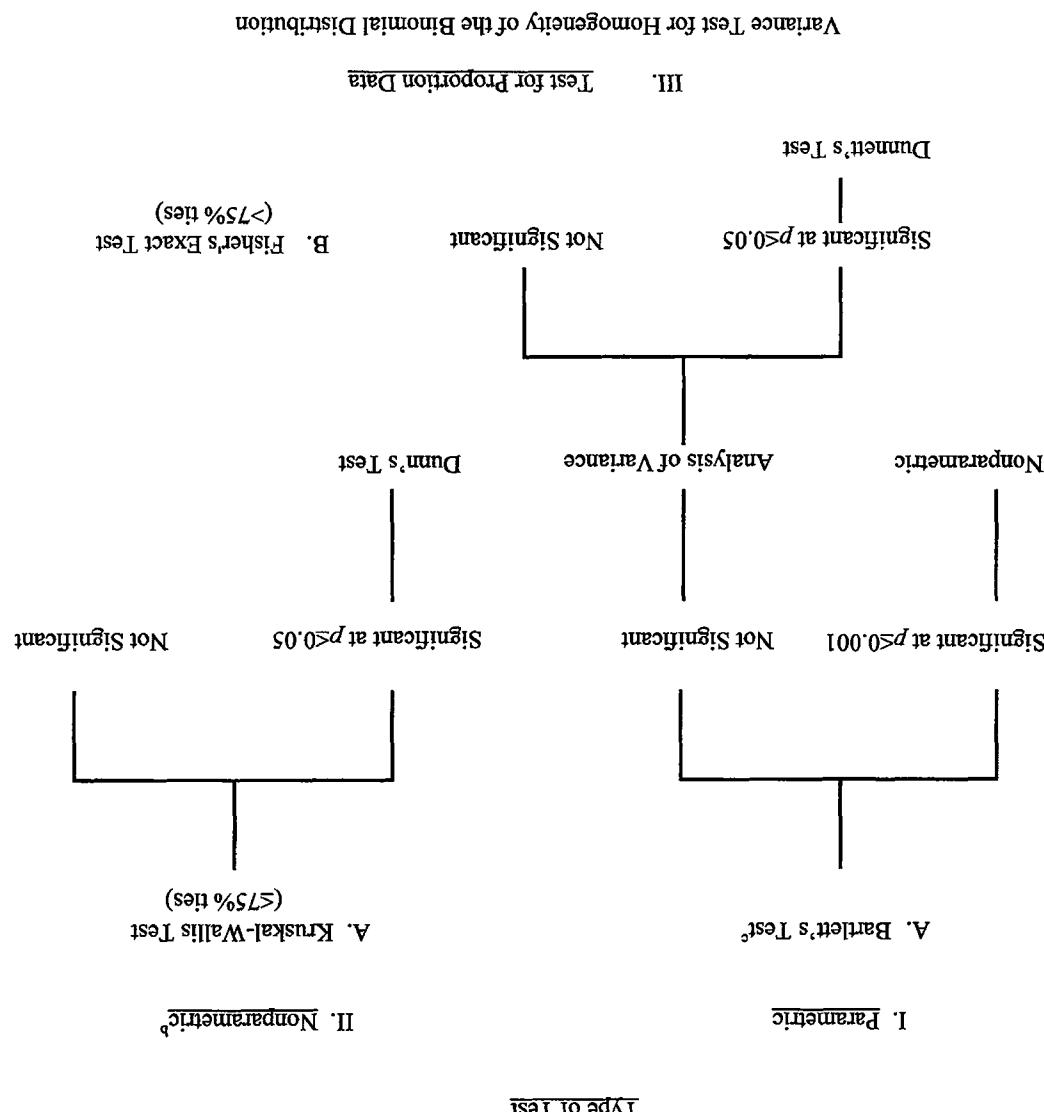
Data generated during the course of this study were recorded either by hand or using the Argus Automated Data Collection and Management System and the Vivarium Temperature and Relative Humidity Monitoring System. Microsoft® Excel (part of Microsoft® Office 97/2000/XP), Quattro Pro 8 and/or summarised and/or statistically analyzed using the Argus Automated Data Collection and Management System, the Vivarium Temperature and Relative Humidity Monitoring System, Microsoft® Excel (part of Microsoft® Office 97/2000/XP), Quattro Pro 8 and/or The SAS System (version 6.12).

2.6.7. Data Collection and Statistical Analyses

Each fetus was removed from the uterus, placed in an individual container and individually identified with a tag noting the study number, litter number, uterine distribution and fixative. Each fetus was subsquently weighed and examined for sex and gross external alterations. Live fetuses were sacrificed by an intraperitoneal injection of sodium pentobarbital. Approximately one-half of the fetuses in each litter were examined for soft tissue alterations using a variation of the adaptation of Wilson's sectioning technique⁽⁹⁾. These fetuses were initially fixed in Bouin's solutions; sections were retained in alcohol. The remaining fetuses (approximately one-half of the fetuses in each litter) were eviscerated, cleared, stained with alizarin red S⁽¹⁰⁾ and examined for skeletal alterations. The fetuses were initially fixed in alcohol. Skeletal preparations were retained in glycerin with glycerol added as a preservative.

by the degree of autolysis present; marked to extreme autolysis indicated that the fetus was a late resorption. Placentae were examined for size, color and shape.

- a. Statistically significant probabilities are reported as either $p \leq 0.05$ or $p \leq 0.01$.
 b. Proportion data are not included in this category.
 c. Test for homogeneity of variance.
-



The following schematic represents the statistical analyses of the data:
 Averages and percentages were calculated. Litter values were used where appropriate.

Clinical observations and other proportional data were analyzed using the Variance Test for Homogeneity of the Binomial Distribution⁽¹¹⁾.

Continuous data (e.g., body weights, body weight changes, feed consumption values, and fecal anomalies) were analyzed using Bartlett's Test of Homogeneity of Variances⁽¹²⁾ and the Analysis of Variance⁽¹³⁾, when appropriate [i.e., Bartlett's Test was not significant ($p > 0.01$)]. If the Analysis of Variance was significant ($p \leq 0.05$), Dunnett's Test⁽¹⁴⁾ was used to identify the statistical significance of the individual groups. If the Analysis of Variance was not appropriate [i.e., Bartlett's Test was present, In cases where the Kruskal-Wallis Test was not applicable significant ($p \leq 0.001$)], the Kruskal-Wallis Test⁽¹⁵⁾ was used, when less than or equal to 75% ties were present. In cases where the Kruskal-Wallis Test was statistically significant ($p \leq 0.05$), Dunn's Method of Multiple Comparisons⁽¹⁶⁾ was used to identify the statistical significance of the individual groups. If there were greater than 75% ties, Fischer's Exact Test⁽¹⁷⁾ was used to analyze the data.

Count data obtained at Caesarean-sectioning of the dams were evaluated using the procedures described above for the Kruskal-Wallis Test⁽¹⁵⁾.

feed consumption values in the 250, 500 and 1000 mg/kg/day dosage groups were 107%, (calculated as DGs 7 to 18), in comparison to the vehicle control group values. Absolute reduced ($p \leq 0.01$) in the 1000 mg/kg/day dosage group during the dosage period Absolute (g/day) and relative (g/kg/day) feed consumption values were significantly ($p \leq 0.01$) in the 1000 mg/kg/day dosage group during the dosage period.

(Summaries - Tables 4 and 5; Individual Data - Table 16)

3.4. Material Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values

of the vehicle control group in the three respective dimyrcetol dosage groups, 95%, respectively, of the vehicle control group value during the dosage period (calculated as DGs 7 to 18). The average material body weight on DG 21 was 99%, 102% and 98% weight gains in the 250, 500 and 1000 mg/kg/day dosage groups were 105%, 110% and days of dosage, but these reductions did not persist throughout the dosage period. Body weight gains were reduced in the 1000 mg/kg/day dosage group for the first few days of dosage, but these reductions did not persist throughout the dosage period. Body

(Figure 1; Summaries - Tables 2 and 3; Individual Data - Table 15)

3.3. Material Body Weights and Body Weight Changes

No gross lesions were revealed by necropsy.

All clinical observations were considered unrelated to dimyrcetol because: 1) the incidences were not dosage-dependent; or 2) the observations were transient and did not persist. These clinical observations included sparse hair coat, excess salivation (slight, moderate and/or extreme), urine-stained abdominal fur, ungrinned coat, rales, presence of a scab on the left side of the back, pustules, localized alopecia on the limbs or underside, chromodacryorrhea, soft or liquid feces and a mass on the right flank.

All rats survived until scheduled sacrifice.

(Summary - Table 1; Individual Data - Tables 13 and 14)

3.2. Mortality, Clinical and Necropsy Observations

The results of the concentration analyses from the start and end of study revealed that all prepared formulations were acceptable for use and within the acceptable limits of $\pm 15\%$. All homogeneity results were within the acceptable range of $\leq 5\%$ relative standard deviation (RSD). The results of the homogeneity analysis were 0.3%, 0.4% and 0.5%. RSD for the 25 mg/mL, 50 mg/mL and 100 mg/mL formulations, respectively. Stability of the prepared formulations bracketing the range of concentrations and storage conditions (22±5°C, protected from light) used in this study were confirmed for 10 days in Charles River Laboratories Preclinical Services, Massachusetts project TIF00010AX.

(APPENDIX E)

3.1. Analytical

3. RESULTS

a. See APPENDIX G (HISTORICAL CONTROL DATA).

Fetal alterations were defined as: 1) malformations (irreversible changes that occur at low incidences in this species and strain); or 2) variations (common findings in this species and strain and reversible delays or accelerations in development). Litter averages were calculated for specific fetal ossification sites as part of the evaluation of the degree of fetal ossification.

3.6. Fetal Alterations (Summaries - Tables 8 through 12; Individual Data - Table 20)

No other Caesarean-sectioning or litter parameters were affected by dosages of dimyrectol as high as 1000 mg/kg/day. The litter averages for corpora lutea, implantations, litter sizes, live fetuses, early and late resorptions, percent resorbed conceptuses, and percent live male fetuses were comparable among the four dosage groups and did not significantly differ. No dam had a litter consisting of only resorbed conceptuses, and there were no dead fetuses. All placenta appeared normal.

No other Caesarean-sectioning or litter parameters were affected by dosages of dimyrectol as high as 1000 mg/kg/day. The litter averages for corpora lutea, implantations, litter sizes, live fetuses, early and late resorptions, percent resorbed conceptuses were within the historical control values for the Testing Facility^a, the reduction correlated with the slight reductions in maternal body weight gain that occurred on the first few days of dosage and the reductions in fetal ossification site averages (see below).

Although the values were within the historical control values for the Testing Facility^a, the group value. A significant reduction ($p \leq 0.05$) in the female fetal body weights occurred. Fetal weights for both male and female fetuses combined were reduced (approximately 3%) in the 1000 mg/kg/day dosage group compared to the concurrent vehicle control.

Pregnancy occurred in 22 to 25 rats per dosage group. Caesarean-sectioning observations on DG 21 were based on 22, 24, and 25 pregnant rats with one or more live fetuses in the 0 (Vehicle), 250, 500 and 1000 mg/kg/day dosage groups, respectively.

3.5. Caesarean-Sectioning and Litter Observations (Summaries - Tables 6 and 7; Individual Data - Tables 17 through 19)

Absolute and relative feed consumption values were unaffected by dosages of dimyrectol as high as 500 mg/kg/day. Despite feed consumption values that were comparable to vehicle control group values during the postdosage period (DGs 18 to 21), absolute and relative feed consumption values remained significantly reduced ($p \leq 0.05$) for the entire gestation period (DGs 7 to 21 and DGs 0 to 21), in comparison to the vehicle control group values.

The dosage period, absolute and relative feed consumption values were significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) in the 1000 mg/kg/day dosage group on DGs 7 to 10 and DGs 10 to 12, as compared with the vehicle control group value. These reductions correlated with reductions in body weights during the first few days of the dosage period.

102% and 87%, respectively, of the vehicle control group value on DGs 7 to 18. Within

3.6. Fetal Alterations

3.6. Fetal Alterations (Summaries - Tables 8 through 12; Individual Data - Table 20)

No other Caesarean-sectioning or litter parameters were affected by dosages of dimyrectol as high as 1000 mg/kg/day. The litter averages for corpora lutea, implantations, litter sizes, live fetuses, early and late resorptions, percent resorbed conceptuses, and percent live male fetuses were comparable among the four dosage groups and did not significantly differ. No dam had a litter consisting of only resorbed conceptuses, and there were no dead fetuses. All placenta appeared normal.

No other Caesarean-sectioning or litter parameters were affected by dosages of dimyrectol as high as 1000 mg/kg/day. The litter averages for corpora lutea, implantations, litter sizes, live fetuses, early and late resorptions, percent resorbed conceptuses were within the historical control values for the Testing Facility^a, the reduction correlated with the slight reductions in fetal ossification site averages (see below).

Although the values were within the historical control values for the Testing Facility^a, the group value. A significant reduction ($p \leq 0.05$) in the female fetal body weights occurred. Fetal weights for both male and female fetuses combined were reduced (approximately 3%) in the 1000 mg/kg/day dosage group compared to the concurrent vehicle control.

Pregnancy occurred in 22 to 25 rats per dosage group. Caesarean-sectioning observations on DG 21 were based on 22, 24, and 25 pregnant rats with one or more live fetuses in the 0 (Vehicle), 250, 500 and 1000 mg/kg/day dosage groups, respectively.

3.5. Caesarean-Sectioning and Litter Observations (Summaries - Tables 6 and 7; Individual Data - Tables 17 through 19)

Absolute and relative feed consumption values were unaffected by dosages of dimyrectol as high as 500 mg/kg/day. Despite feed consumption values that were comparable to vehicle control group values during the postdosage period (DGs 18 to 21), absolute and relative feed consumption values remained significantly reduced ($p \leq 0.05$) for the entire gestation period (DGs 7 to 21 and DGs 0 to 21), in comparison to the vehicle control group values.

The dosage period, absolute and relative feed consumption values were significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) in the 1000 mg/kg/day dosage group on DGs 7 to 10 and DGs 10 to 12, as compared with the vehicle control group value. These reductions correlated with reductions in body weights during the first few days of the dosage period.

102% and 87%, respectively, of the vehicle control group value on DGs 7 to 18. Within

No other fetal gross external alterations (malformations or variations) occurred. One fetus (11493-9) in the 1000 mg/kg/day dosage group had a thread-like tail. Skeletal examination confirmed the gross external alteration by revealing the presence of two sacral vertebrae and the absence of any caudal vertebrae. No other alterations occurred in this fetus.

3.6.2.2. Tail

Fetus 11401-8 in the vehicle control group had an abdominal wall defect (i.e., gastroschisis) through which a portion of the small intestine protruded. Soft tissue fistulas protruding through the umbilicus. No other alterations occurred in this fetus.

3.6.2.1. Body

(Summary - Table 9; Individual Data - Table 20)

All fetal alterations in this study are described in the following information. In Groups I through IV, litter numbers with alterations numbered 8 (36.4%), 5 (20.8%), 6 (25.0%) and 12 (48.0%), respectively. The numbers of fetuses with any alteration observed were 12 (4.1%), 8 (2.6%), 6 (1.7%) and 15 (4.2%). In Groups V through VIII, litter numbers with alterations numbered 8 (36.4%), 5 (20.8%), 6 (25.0%) and 12 (48.0%), respectively. The numbers of fetuses with any alteration observed per litter were 4,0%, 2.5%, 1.8% and 4.3% in these same respective dosage groups.

(Summary - Table 8; Individual Data - Table 20)

The 1000 mg/kg/day dosage group had increases in the incidence of supernumerary thoracic ribs with associated significant increases and decreases ($p \leq 0.05$ or $p \leq 0.01$) in the numbers of thoracic and lumbar vertebrae, respectively. There was also a significant reduction ($p \leq 0.01$) in the average number of ossified hindlimb metatarsals in the same groups. In Groups I through IV, litters with fetuses with alterations numbered 8 (36.4%), 5 (20.8%), 6 (25.0%) and 12 (48.0%), respectively. The numbers of fetuses with any alteration observed per litter were 4,0%, 2.5%, 1.8% and 4.3% in these same respective dosage groups.

Fetal evaluations were based on 295, 311, 350 and 358 live DG 21 Cesarean-delivered fetuses in 22, 24, 24 and 25 litters in the 0 (Vehicle), 250, 500 and 1000 mg/kg/day dosage groups, respectively. Each of these fetuses was examined for gross external soft tissue alterations. Of these respecitive fetuses, 140, 147, 167 and 174 fetuses were examined for skeletal alterations. Of these respecitive fetuses, 155, 164, 183 and 184 fetuses were examined for skeletal alterations and fetal ossification site averages.

Skeletal examination of fetuses 11493-9 in the 1000 mg/kg/day dosage group confirmed the grossly observed thread-like tail, by revealing the absence of caudal vertebrae and an

3.6.4.1.1. Vertebrae

3.6.4.1. Malformations

(Summary - Table 10; Individual Data - Table 20)

3.6.4. Fetal Skeletal Alterations

No other soft tissue variations occurred.

Slight dilation of the renal pelvis of one or both kidneys, a reversible developmental delay⁽¹⁹⁾, occurred in two fetuses (11482-9 and 11483-12) from two litters in the 1000 mg/kg/day dosage group. No other alterations occurred in these fetuses.

3.6.3.2.3. Kidneys

The umbilical artery descended to the left of the urinary bladder in 0, 2, 4 and 1 fetuses from 0, 2, 4 and 1 litters in the 0 (Vehicle), 250, 500 and 1000 mg/kg/day dosage groups, respectively. No other alterations occurred in these fetuses.

The innominate artery was absent in fetus 11414-10 in the vehicle control group. No other alterations occurred in this fetus.

3.6.3.2.2. Vessels

Fetus 11488-4 in the 1000 mg/kg/day dosage group had a folded retina of the left eye, a common variation in this strain of rat. No other alterations occurred in this fetus.

3.6.3.2.1. Eyes

3.6.3.2. Variations

No other soft tissue malformations occurred.

Soft tissue examination of fetus 11401-8 in the 0 (Vehicle) mg/kg/day dosage group confirmed the presence of an abdominal wall defect, as previously described.

3.6.3.1.1. Intestines

3.6.3.1. Malformations

(Summary - Table 10; Individual Data - Table 20)

3.6.3. Fetal Soft Tissue Alterations

3

3.6.4.1.2. Ribs

irregular number of sacral vertebrae present (two rather than three for this species). This fetus was fully described in section 1.5.2.2.

Three fetuses (11405-16 and 11412-7 and -13) from two litters in the vehicle control group had short ribs as their only alteration. The significant reduction ($p \leq 0.01$) in the occurrence of short ribs in the 250, 500 and 1000 mg/kg/day dosage group was considered unrelated to dimyrcetol because: 1) an increase rather than a decrease would be the expected effect of a developmental toxicant; 2) the incidence were not dosage-dependent; and 3) the litter incidence, the more important parameter⁽¹⁾, was not statistically different from vehicle control group values.

No other skeletal malformations occurred.

3.6.4.2. Variations

The presence of a cervical rib at the 7th cervical vertebra, a common variation in this strain of rat⁽¹⁹⁾, occurred in 1, 5, 1 and 5 fetuses from 1, 3, 1 and 4 litters in the 0 (Vehicle), 250, 500 and 1000 mg/kg/day dosage groups, respectively. No additional alterations occurred in these fetuses.

3.6.4.2.2. Thoracic Vertebrae

A bifid centrum in a thoracic vertebra occurred in 4, 1, 0 and 2 fetuses from 4, 1, 0 and 2 litters in the 0 (Vehicle), 250, 500 and 1000 mg/kg/day dosage groups, respectively. No additional alterations occurred in these fetuses.

3.6.4.2.3. Lumbar Vertebrae

Unilateral ossification of the centrum in the last lumbar vertebra occurred in one fetus (11500-5) in the 1000 mg/kg/day dosage group. No other alterations occurred in this fetus.

3.6.4.2.4. Ribs

Wavy ribs, a reversible delay in ossification⁽²⁰⁾, occurred in two fetuses from the same litter (11417-5 and 11417-11) in the 0 (Vehicle) mg/kg/day dosage group. No additional alterations occurred in these fetuses.

The 1000 mg/kg/day dosage group had increases in the incidence of supernumerary thoracic ribs with associated significant increases and decreases ($p \leq 0.05$ or $p \leq 0.01$) in the numbers of thoracic and lumbar vertebrae, respectively, a common variation observed at maternally toxic doses⁽²¹⁾. There was also a significant reduction ($p \leq 0.01$) in the average number of ossified hindlimb metatarsals in the 1000 mg/kg/day dosage group. There were no statistically significant or biologically important differences among the four dosage groups in the average numbers of ossification sites per fetus for the hyoid, vertebral (cervical, sacral and caudal), sternum (manubrium, sternal centra and xiphoid), forelimbs (carpal, metacarpals, and phalanges) or hindlimbs (tarsals and phalanges).

3.6.4.2.6. Fetal Ossification Site Averages

Delayed sternal ossification (incomplete ossified 1st sternal centra) occurred in two fetuses (11476-4 and 11499-1) in the 1000 mg/kg/day dosage group. No additional alterations occurred in these fetuses.

Fetuses 11467-14 in the 500 mg/kg/day dosage group had fused sternal centra (2nd through 4th). This fetus also had asymmetric sternal centra (2nd and 3rd). No additional alterations occurred in this fetus.

3.6.4.2.5. Sternum

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PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 1 (PAGE 1): CLINICAL AND NECROPSY OBSERVATIONS - SUMMARY

	I 0 (VEHICLE)	II 250	III 500	IV 1,000
MAXIMUM POSSIBLE INCIDENCE	375/ 25	375/ 25	375/ 25	375/ 25
MORTALITY	0	0	0	0
SPARSE HAIR COAT	23/ 4	5/ 1	16/ 2	61/ 6
EXCESS SALIVATION - SLIGHT, MODERATE AND/OR EXTREME	1/ 1	0/ 0	1/ 1	5/ 4
URINE-STAINED ABDOMINAL FUR	3/ 1	0/ 0	2/ 2	2/ 1
UNGROOMED COAT	0/ 0	0/ 0	0/ 0	1/ 1
RALES	0/ 0	0/ 0	0/ 0	1/ 1
LEFT SIDE OF BACK: SCAB	0/ 0	0/ 0	0/ 0	1/ 1
PTOSIS	0/ 0	0/ 0	0/ 0	1/ 1
LOCALIZED ALOPECIA:	TOTAL LIMB(S) UNDERSIDE	31/ 4 31/ 4 0/ 0	7/ 1 0/ 0 7/ 1	15/ 2 15/ 2 0/ 0
CHROMODACRYORRHEA	1/ 1	0/ 0	3/ 1	0/ 0
SOFT OR LIQUID FECES	0/ 0	1/ 1	1/ 1	0/ 0
RIGHT FLANK: MASS	0/ 0	5/ 1	0/ 0	0/ 0

PERSISTENT ADVERSE CLINICAL OBSERVATIONS WERE CONFIRMED AT NECROPSY, NO ADDITIONAL GROSS LESIONS WERE IDENTIFIED

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.
 MAXIMUM POSSIBLE INCIDENCE = (DAYS X RATES)/NUMBER OF RATS EXAMINED PER GROUP ON DAYS 7 THROUGH 21 OF PRESUMED GESTATION.
 N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.

- a. Dosage occurred on days 7 through 17 of presumed gestation.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 2 (PAGE 1): MATERNAL BODY WEIGHTS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY) a	RATS TESTED	I 0 (VEHICLE)			II 250			III 500			IV 1,000		
		N	25	25	N	24	24	N	25	25	N	25	25
MATERNAL BODY WEIGHT (G)													
DAY 0	MEAN±S.D.	230.8 ± 6.7	230.5 ± 6.8	231.0 ± 6.6	230.6 ± 7.1								
DAY 7	MEAN±S.D.	273.4 ± 10.5	272.5 ± 10.4	271.7 ± 13.3	270.4 ± 10.4								
DAY 8	MEAN±S.D.	270.8 ± 11.0	272.1 ± 10.9	270.4 ± 13.5	266.3 ± 11.6								
DAY 9	MEAN±S.D.	272.2 ± 10.7	274.1 ± 12.0	272.0 ± 14.6	265.2 ± 11.1								
DAY 10	MEAN±S.D.	275.4 ± 11.2	278.0 ± 12.0	278.1 ± 15.3	270.6 ± 13.0								
DAY 11	MEAN±S.D.	283.4 ± 12.4	285.8 ± 12.9	285.5 ± 16.2	277.0 ± 15.2								
DAY 12	MEAN±S.D.	287.4 ± 12.8	292.8 ± 12.8	291.0 ± 17.8	282.4 ± 17.4								
DAY 13	MEAN±S.D.	293.0 ± 14.2	296.3 ± 14.4	296.2 ± 17.0	288.7 ± 19.8								
DAY 14	MEAN±S.D.	297.0 ± 15.5	302.7 ± 16.0	302.2 ± 17.7	293.8 ± 16.8								
DAY 15	MEAN±S.D.	305.1 ± 16.6	309.9 ± 17.1	310.8 ± 19.2	300.8 ± 17.7								
DAY 16	MEAN±S.D.	317.4 ± 17.3	320.6 ± 19.0	320.5 ± 20.6	311.9 ± 17.3								
DAY 17	MEAN±S.D.	329.8 ± 19.9	334.8 ± 19.3	334.8 ± 22.8	326.0 ± 19.3								
DAY 18	MEAN±S.D.	346.3 ± 21.4	349.3 ± 21.0	352.0 ± 24.1	339.7 ± 19.4								
DAY 19	MEAN±S.D.	361.9 ± 23.4	363.2 ± 21.1	368.8 ± 25.8	354.0 ± 20.5								
DAY 20	MEAN±S.D.	378.2 ± 25.2	378.1 ± 22.6	385.6 ± 28.0	370.6 ± 23.9								
DAY 21	MEAN±S.D.	405.7 ± 27.8	403.4 ± 23.0	412.9 ± 29.9	397.8 ± 26.0								

DAY = DAY OF GESTATION

a. Dosage occurred on days 7 through 17 of gestation.

PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 3 (PAGE 1): MATERNAL BODY WEIGHT CHANGES - SUMMARY

RATS TESTED	N	DOSE GROUP			DOSE (MG/KG/DAY) a			MATERNAL BODY WEIGHT CHANGE (G)		
		I 0 (VEHICLE)	II 250	III 500	IV 1000	25	25	25	24	24
PREGNANT	N	22	22	24	24					
DAYS 0 - 7	MEAN±S.D.	+42.5 ± 7.2	+42.0 ± 8.2	+40.7 ± 10.6	+39.8 ± 7.5					
DAYS 7 - 10	MEAN±S.D.	+2.0 ± 6.5	+5.5 ± 7.0	+6.4 ± 8.6	+0.1 ± 9.4					
DAYS 10 - 12	MEAN±S.D.	+12.0 ± 5.3	+14.8 ± 5.4	+12.9 ± 5.2	+11.8 ± 9.6					
DAYS 12 - 15	MEAN±S.D.	+17.7 ± 8.5	+17.1 ± 9.5	+19.8 ± 5.8	+18.4 ± 7.3					
DAYS 15 - 18	MEAN±S.D.	+41.2 ± 9.6	+39.4 ± 8.8	+41.2 ± 7.3	+39.0 ± 7.7					
DAYS 7 - 18	MEAN±S.D.	+73.0 ± 17.0	+76.8 ± 15.2	+80.2 ± 14.5	+69.3 ± 15.1					
DAYS 18 - 21	MEAN±S.D.	+59.4 ± 11.4	+54.2 ± 8.7	+61.0 ± 10.8	+58.1 ± 12.8					
DAYS 7 - 21	MEAN±S.D.	+132.4 ± 22.6	+130.9 ± 16.7	+141.2 ± 20.5	+127.4 ± 20.5					
DAYS 0 - 21	MEAN±S.D.	+174.9 ± 25.6	+173.0 ± 21.0	+181.9 ± 27.2	+167.2 ± 23.6					

DAYS = DAYS OF GESTATION

a. Dosage occurred on days 7 through 17 of gestation.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 4 (PAGE 1): MATERNAL ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - SUMMARY

RATS TESTED	PREGNANT	N	MATERNAL FEED CONSUMPTION (G/DAY)	I 0 (VEHICLE)		II 250		III 500		IV 1000	
				25	25	25	25	25	25	25	25
DOSE GROUP DOSE (MG/KG/DAY) a											
DAYS 0 - 7	MEAN±S.D.	24.3 ± 2.0		23.7 ± 2.2		23.6 ± 3.2		23.2 ± 2.0			
DAYS 7 - 10	MEAN±S.D.	16.0 ± 3.1		[23] b	16.7 ± 3.1	[23] b	16.5 ± 3.9	[23] b	12.4 ± 3.2**		
DAYS 10 - 12	MEAN±S.D.	17.4 ± 3.2		18.7 ± 2.8		17.2 ± 2.9		17.2 ± 2.9		15.1 ± 4.3*	
DAYS 12 - 15	MEAN±S.D.	17.7 ± 2.4		19.2 ± 3.4		17.9 ± 2.7		16.0 ± 3.1			
DAYS 15 - 18	MEAN±S.D.	20.8 ± 4.9		[22] b	22.6 ± 3.2	[23] b	21.3 ± 4.0	[23] b	19.4 ± 2.8		
DAYS 7 - 18	MEAN±S.D.	18.1 ± 2.1		19.3 ± 2.4		18.4 ± 2.8		15.8 ± 2.1**			
DAYS 18 - 21	MEAN±S.D.	[21] b	27.3 ± 3.8	26.8 ± 3.3		28.4 ± 3.7		27.9 ± 3.4			
DAYS 7 - 21	MEAN±S.D.	20.0 ± 2.1		21.0 ± 2.3		20.6 ± 2.8		18.4 ± 2.0*			
DAYS 0 - 21	MEAN±S.D.	21.4 ± 1.8		21.9 ± 2.0		21.6 ± 2.6		20.0 ± 1.7*			

DOYS = DAYS OF GESTATION

[] = NUMBER OF VALUES AVERAGED

a. Dosage occurred on days 7 through 17 of gestation.

b. Excludes values that could not be calculated, appeared incorrectly recorded, and/or those associated with spillage.

* Significantly different from the vehicle control group value ($p \leq 0.05$).

** Significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 5 (PAGE 1): MATERNAL RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - SUMMARY

RATS TESTED	N	PREGNANT	N	MATERNAL FEED CONSUMPTION (G/KG/DAY)		I 0 (VEHICLE) 25	II 1 250 500 25	III 500 25	IV 1000 25
				I	IV				
DAY 0 - 7	MEAN±S.D.	96.2 ± 6.8		94.2 ± 6.9		93.5 ± 10.6		92.5 ± 6.5	
DAY 7 - 10	MEAN±S.D.	58.6 ± 10.2		60.8 ± 9.7		[23] b 60.4 ± 12.7		46.2 ± 11.3*	
DAY 10 - 12	MEAN±S.D.	61.4 ± 9.6		65.4 ± 8.8		[23] b 60.0 ± 7.9		54.2 ± 15.5*	
DAY 12 - 15	MEAN±S.D.	59.8 ± 7.2		63.5 ± 9.7		59.6 ± 7.1		54.9 ± 9.3	
DAY 15 - 18	MEAN±S.D.	63.8 ± 14.0		68.7 ± 7.6		[23] b 64.2 ± 10.0		60.8 ± 8.9	
DAY 7 - 18	MEAN±S.D.	61.0 ± 5.6		64.5 ± 6.0		61.4 ± 7.3		54.1 ± 6.1*	
DAY 18 - 21	MEAN±S.D.	73.1 ± 8.1		71.8 ± 8.7		74.6 ± 7.1		76.2 ± 8.1	
DAY 7 - 21	MEAN±S.D.	63.7 ± 4.8		66.4 ± 5.4		64.7 ± 6.0		59.6 ± 5.3*	
DAY 0 - 21	MEAN±S.D.	69.5 ± 4.0		70.5 ± 4.6		69.0 ± 5.3		66.0 ± 3.8*	

DAYS = DAYS OF GESTATION

[] = NUMBER OF VALUES AVERAGED

a. Dosage occurred on days 7 through 17 of gestation.

b. Excludes values that could not be calculated or appeared incorrectly recorded, as well as those associated with spillage.

* Significantly different from the vehicle control group value ($p \leq 0.05$).** Significantly different from the vehicle control group value ($p \leq 0.01$).

TABLE 6 (PAGE 1): CAESAREAN-SECTIONING OBSERVATIONS - SUMMARY

DOSE GROUP DOSE (MG/KG/DAY) a	RATS TESTED	I 0 (VEHICLE)			II 250			III 500			IV 1,000		
		N	25		25		25		25		25		25
PREGNANT RATS PREGNANT AND CAESAREAN-SECTIONED ON DAY 21 OF GESTATION	N (%)	22 (88.0)			24 (96.0)			24 (96.0)			25 (100.0)		
CORPORA LUTEA	MEAN±S.D.	14.6 ± 2.4			14.9 ± 2.8			16.3 ± 2.4			15.8 ± 2.3		
IMPLANTATIONS	MEAN±S.D.	14.0 ± 2.1			13.8 ± 2.8			15.2 ± 1.7			14.8 ± 1.8		
LITTER SIZES	MEAN±S.D.	13.4 ± 2.2			13.0 ± 2.4			14.6 ± 2.0			14.3 ± 2.4		
LIVE FETUSES	N	295			311			350			358		
DEAD FETUSES	MEAN±S.D.	13.4 ± 2.2			13.0 ± 2.4			14.6 ± 2.0			14.3 ± 2.4		
RESORPTIONS	N	0			0			0			0		
EARLY RESORPTIONS	MEAN±S.D.	0.6 ± 0.7			0.8 ± 0.9			0.6 ± 0.6			0.5 ± 1.2		
LATE RESORPTIONS	N	12			20			14			12		
DAMS WITH ANY RESORPTIONS	MEAN±S.D.	0.5 ± 0.7			0.8 ± 0.9			0.6 ± 0.6			0.5 ± 1.2		
DAMS WITH ALL CONCEPTUSES RESORBED	N (%)	10 (45.4)			12 (50.0)			13 (54.2)			7 (28.0)		
DAMS WITH VISIBLE FETUSES	N (%)	22 (100.0)			24 (100.0)			24 (100.0)			25 (100.0)		
PLACENTAE APPEARED NORMAL	N (%)	22 (100.0)			24 (100.0)			24 (100.0)			25 (100.0)		

a. Dosage occurred on days 7 through 17 of gestation.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 7 (PAGE 1): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - SUMMARY

DOSAGE GROUP DOSE (MG/KG/DAY) a	I 0 (VEHICLE)	II 250	III 500	IV 1000
LITTERS WITH ONE OR MORE LIVE FETUSES	N MEAN±S.D.	22 14.0 ± 2.1	24 13.8 ± 2.8	24 15.2 ± 1.7
IMPLANTATIONS	N MEAN±S.D.	295 13.4 ± 2.2	311 13.0 ± 2.4	350 14.6 ± 2.0
LIVE FETUSES	N MEAN±S.D.	140	145	179
LIVE MALE FETUSES	N MEAN±S.D.			192
% LIVE MALE FETUSES/LITTER	MEAN±S.D.	47.2 ± 10.7	47.6 ± 18.4	51.1 ± 12.2
LIVE FETAL BODY WEIGHTS (GRAMS)/LITTER	MEAN±S.D.	5.50 ± 0.28	5.54 ± 0.30	5.55 ± 0.31
MALE FETUSES	MEAN±S.D.	5.63 ± 0.28	5.73 ± 0.31	5.68 ± 0.28
FEMALE FETUSES	MEAN±S.D.	5.38 ± 0.29	5.37 ± 0.28 [23] b	5.42 ± 0.35
% RESORBED CONCEPTUSES/LITTER	MEAN±S.D.	4.2 ± 5.3	5.5 ± 6.1	4.0 ± 4.1
				3.5 ± 9.4

[] = NUMBER OF VALUES AVERAGED

a. Dosage occurred on days 7 through 17 of gestation.

b. Litter 11440 had no female fetuses.

* Significantly different from the vehicle control group value ($p \leq 0.05$).

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 8 (PAGE 1): FETAL ALTERATIONS - SUMMARY

DOSE GROUP DOSE (MG/KG/DAY) a	I 0 (VEHICLE)	II 250	III 500	IV 1000
LITTERS EVALUATED	N 22	24	24	25
FETUSES EVALUATED	N 295	311	350	358
LIVE	N 295	311	350	358
LITTERS WITH FETUSES WITH ANY ALTERATION OBSERVED	N(%) 8(36.4)	5(20.8)	6(25.0)	12(48.0)
FETUSES WITH ANY ALTERATION OBSERVED	N(%) 12(4.1)	8(2.6)	6(1.7)	15(4.2)
% FETUSES WITH ANY ALTERATION/LITTER	MEAN±S.D. 4.0 ± 6.0	2.5 ± 5.5	1.8 ± 3.1	4.3 ± 5.6

a. Dosage occurred on days 7 through 17 of gestation.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 9 (PAGE 1): FETAL GROSS EXTERNAL ALTERATIONS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY) a	LITTERS EVALUATED	FETUSES EVALUATED	LIVE	0 (VEHICLE)		I		II		III		IV	
				N	N	N	N	22	250	24	500	25	1000
BODY: GASTROSCHISIS													
LITTER INCIDENCE	N (%)	1 (4.5)				0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	
FETAL INCIDENCE	N (%)	1 (0.3)				0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	
TAIL: THREAD-LIKE													
LITTER INCIDENCE	N (%)	0 (0.0)				0 (0.0)		0 (0.0)		0 (0.0)		1 (4.0)	
FETAL INCIDENCE	N (%)	0 (0.0)				0 (0.0)		0 (0.0)		0 (0.0)		1 (0.3)	

a. Dosage occurred on days 7 through 17 of gestation.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 10 (PAGE 1): FETAL SOFT TISSUE ALTERATIONS - SUMMARY

DOSAGE GROUP DOSE (MG/KG/DAY) a	I 0 (VEHICLE)	II 250	III 500	IV 1000
LITTERS EVALUATED	N N N	22 140 140	24 147 147	24 167 167
FETUSES EVALUATED				25 174 174
LIVE	N			
EYES: RETINA FOLDED	N (%) N (%)	0(0.0) 0(0.0)	0(0.0) 0(0.0)	0(0.0) 0(0.0)
FETAL INCIDENCE				1(4.0) 1(0.6)
VESSELS: UMBILICAL ARTERY DESCENDS TO LEFT OF URINARY BLADDER	N (%) N (%)	0(0.0) 0(0.0)	2(8.3) 2(14.4)	4(16.7) 4(2.4)
FETAL INCIDENCE	N (%) N (%)	0(0.0) 0(0.0)		1(4.0) 1(0.6)
VESSELS: INNOMINATE ARTERY ABSENT	N (%) N (%)	1(4.5) 1(0.7)	0(0.0) 0(0.0)	0(0.0) 0(0.0)
FETAL INCIDENCE	N (%) N (%)			0(0.0) 0(0.0)
KIDNEYS: PELVIS, SLIGHT DILATION	N (%) N (%)	0(0.0) 0(0.0)	0(0.0) 0(0.0)	0(0.0) 0(0.0)
FETAL INCIDENCE	N (%) N (%)			2(8.0) 2(1.1)
INTESTINES: PORTION OF INTESTINE PROTRUDING THROUGH UMBILICUS	N (%) N (%)	1(4.5) 1(0.7)	0(0.0) 0(0.0)	0(0.0) 0(0.0)
FETAL INCIDENCE	N (%) N (%)			

a. Dosage occurred on days 7 through 17 of presumed gestation.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS
 TABLE 11 (PAGE 1): FETAL SKELETAL ALTERATIONS - SUMMARY
 (See footnotes on the last page of this table.)

DOSAGE GROUP DOSE (MG/KG/DAY) a	0 (VEHICLE)	I		II		III		IV	
		250	500	24	164	183	183	1000	
LITTERS EVALUATED	N	22		24		24		25	
FETUSES EVALUATED	N	155		164		183		184	
LIVE	N	155		164		183		184	
CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA									
LITTER INCIDENCE	N(%)	1(4.5)		3(12.5)		1(4.2)		4(16.0)	
FETAL INCIDENCE	N(%)	1(0.6)		5(3.0)		1(0.5)		5(2.7)	
THORACIC VERTEBRAE: CENTRUM, BIFID									
LITTER INCIDENCE	N(%)	4(18.2)		1(4.2)		0(0.0)		2(8.0)	
FETAL INCIDENCE	N(%)	4(2.6)		1(0.6)		0(0.0)		2(1.1)	
LUMBAR VERTEBRAE: CENTRUM, UNILATERAL OSSIFICATION									
LITTER INCIDENCE	N(%)	0(0.0)		0(0.0)		0(0.0)		1(4.0)	
FETAL INCIDENCE	N(%)	0(0.0)		0(0.0)		0(0.0)		1(0.5)	
SACRAL VERTEBRAE: 2 PRESENT									
LITTER INCIDENCE	N(%)	0(0.0)		0(0.0)		0(0.0)		1(4.0)	
FETAL INCIDENCE	N(%)	0(0.0)		0(0.0)		0(0.0)		1(0.5)c	
CAUDAL VERTEBRAE: 0 PRESENT									
LITTER INCIDENCE	N(%)	0(0.0)		0(0.0)		0(0.0)		1(4.0)	
FETAL INCIDENCE	N(%)	0(0.0)		0(0.0)		0(0.0)		1(0.5)c	
RIBS: SHORT									
LITTER INCIDENCE	N(%)	2(9.1)		0(0.0)		0(0.0)		0(0.0)	
FETAL INCIDENCE	N(%)	3(1.9)		0(0.0)**		0(0.0)**		0(0.0)**	
RIBS: WAVY									
LITTER INCIDENCE	N(%)	1(4.5)		0(0.0)		0(0.0)		0(0.0)	
FETAL INCIDENCE	N(%)	2(1.3)		0(0.0)		0(0.0)		0(0.0)	

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 11 (PAGE 2): FETAL SKELETAL ALTERATIONS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY) a	I 0 (VEHICLE)	II 250		III 500		IV 1000	
		LITTERS EVALUATED	FETUSES EVALUATED	LITTERS EVALUATED	FETUSES EVALUATED	LITTERS EVALUATED	FETUSES EVALUATED
STERNAL CENTRA: FUSED							
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.2)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)	0(0.0)
STERNAL CENTRA: ASYMMETRIC							
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.2)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)	0(0.0)
STERNAL CENTRA: INCOMPLETELY OSSIFIED							
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(8.0)	2(1.1)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(1.1)	2(1.1)

a. Dosage occurred on days 7 through 17 of gestation.

b. Fetus 11467-14 had other skeletal alterations.

c. Fetus 11493-9 had other skeletal alterations.

** Significantly different from the vehicle control group value ($p \leq 0.01$).

TABLE 12 (PAGE 1): FETAL OSSIFICATION SITES - CEFASAREAN-DELIVERED LIVE FETUSES (DAY 21 OF GESTATION) - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY) ^a	LITTERS EXAMINED	FETUSES EXAMINED	I (VEHICLE)		II 250		III 500		IV 1000	
			N	N	22	155	24	164	25	184
OSSIFICATION SITES PER FETUS PER LITTER										
HYOID	MEAN±S.D.	1.00 ± 0.00			1.00 ± 0.00		0.99 ± 0.04		1.00 ± 0.00	
VERTEBRAE										
CERVICAL	MEAN±S.D.	7.00 ± 0.00			7.00 ± 0.00		7.00 ± 0.00		7.00 ± 0.00	
THORACIC	MEAN±S.D.	13.08 ± 0.15			13.08 ± 0.16		13.12 ± 0.17		13.24 ± 0.23*	
LUMBAR	MEAN±S.D.	5.92 ± 0.15			5.91 ± 0.16		5.87 ± 0.17		5.75 ± 0.27*	
SACRAL	MEAN±S.D.	3.00 ± 0.00			3.00 ± 0.00		3.00 ± 0.00		3.00 ± 0.00	
CAUDAL	MEAN±S.D.	7.86 ± 0.67			7.84 ± 0.60		7.79 ± 0.78		7.60 ± 0.74	
RIBS (PAIRS)	MEAN±S.D.	13.06 ± 0.11			13.06 ± 0.10		13.09 ± 0.13		13.19 ± 0.23	
STERNUM	MEAN±S.D.	1.00 ± 0.00			1.00 ± 0.00		1.00 ± 0.00		0.99 ± 0.04	
MANUBRIUM	MEAN±S.D.	4.00 ± 0.00			4.00 ± 0.00		4.00 ± 0.00		3.99 ± 0.04	
STERNAL CENTERS	MEAN±S.D.	1.00 ± 0.00			1.00 ± 0.00		1.00 ± 0.00		0.99 ± 0.04	
XIPHOID	MEAN±S.D.									
FORELIMB b										
CARPALS	MEAN±S.D.	0.00 ± 0.00			0.00 ± 0.00		0.00 ± 0.00		0.00 ± 0.00	
METACARPALS	MEAN±S.D.	4.00 ± 0.00			4.00 ± 0.00		4.00 ± 0.00		4.00 ± 0.02	
DIGITS	MEAN±S.D.	5.00 ± 0.00			5.00 ± 0.00		5.00 ± 0.00		5.00 ± 0.00	
PHALANGES	MEAN±S.D.	8.36 ± 0.81			8.32 ± 0.66		8.38 ± 0.52		8.19 ± 0.69	
HINDLIMB b	MEAN±S.D.									
TARSALS	MEAN±S.D.	0.01 ± 0.03			0.01 ± 0.04		0.04 ± 0.14		0.00 ± 0.02	
METATARSALS	MEAN±S.D.	4.95 ± 0.12			4.87 ± 0.21		4.91 ± 0.12		4.78 ± 0.27*	
DIGITS	MEAN±S.D.	5.00 ± 0.00			5.00 ± 0.00		5.00 ± 0.00		5.00 ± 0.00	
PHALANGES	MEAN±S.D.	6.67 ± 1.12			6.28 ± 0.79		6.35 ± 0.98		6.02 ± 0.93	

a. Dosage occurred on days 7 through 17 of gestation.

b. Calculated as average per limb.

* Significantly different from the vehicle control group value ($p \leq 0.05$).** Significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 13 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #	DOSE GROUP I	VEHICLE CONTROL	0 (VEHICLE) MG/KG/DAY	DESCRIPTION	
11401	DG (14- 21)			NO ADVERSE FINDINGS	
11402				SPARSE HAIR COAT a	
11403				NO ADVERSE FINDINGS	
11404				NO ADVERSE FINDINGS	
11405				NO ADVERSE FINDINGS	
11406				NO ADVERSE FINDINGS	
11407	DG (12- 14)			URINE-STAINED ABDOMINAL FUR	
	DG (13- 21)			SPARSE HAIR COAT a	
11408	DG (11- 14)			SPARSE HAIR COAT	
	DG (15- 21)			LOCALIZED ALOPECIA: LIMB (S) a	
11409				NO ADVERSE FINDINGS	
11410	DG (17)			EXCESS SALIVATION - MODERATE	
11411				NO ADVERSE FINDINGS	
11412	DG (21)			LOCALIZED ALOPECIA: LIMB (S) a	
11413				NO ADVERSE FINDINGS	
11414				NO ADVERSE FINDINGS	
11415	DG (7- 21)			LOCALIZED ALOPECIA: LIMB (S) a	
	DG (20- 21)			SPARSE HAIR COAT a	
11416				NO ADVERSE FINDINGS	
11417	DG (12- 19)			NO ADVERSE FINDINGS	
11418	DG (7)			LOCALIZED ALOPECIA: CHROMODACRYOREHEA	
11419				NO ADVERSE FINDINGS	
11420				NO ADVERSE FINDINGS	
11421				NO ADVERSE FINDINGS	
11422				NO ADVERSE FINDINGS	
11423				NO ADVERSE FINDINGS	
11424				NO ADVERSE FINDINGS	
11425				NO ADVERSE FINDINGS	

DG = DAY OF PRESUMED GESTATION

a. Observation confirmed at necropsy.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 13 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #	DOSE GROUP II	LOW DOSE		250 MG/KG/DAY
			DESCRIPTION	
11426			NO ADVERSE FINDINGS	
11427			NO ADVERSE FINDINGS	
11428	DG (17- 21)		NO ADVERSE FINDINGS	
11429			SPARSE HAIR COAT a	
11430			NO ADVERSE FINDINGS	
11431	DG (15- 21)		LOCALIZED ALOPECIA; UNDERSIDE a	
11432			NO ADVERSE FINDINGS	
11433			NO ADVERSE FINDINGS	
11434	DG (17- 21)		RIGHT FLANK: MASS (DID NOT EXCEED 4.0 CM X 2.0 CM X 1.5 CM)b	
11435			NO ADVERSE FINDINGS	
11436			NO ADVERSE FINDINGS	
11437			NO ADVERSE FINDINGS	
11438			NO ADVERSE FINDINGS	
11439			NO ADVERSE FINDINGS	
11440			NO ADVERSE FINDINGS	
11441			NO ADVERSE FINDINGS	
11442			NO ADVERSE FINDINGS	
11443			NO ADVERSE FINDINGS	
11444			NO ADVERSE FINDINGS	
11445			NO ADVERSE FINDINGS	
11446			NO ADVERSE FINDINGS	
11447			NO ADVERSE FINDINGS	
11448			NO ADVERSE FINDINGS	
11449			NO ADVERSE FINDINGS	
11450	DG (10)		SOFT OR LIQUID FECES	

DG = DAY OF PRESUMED GESTATION

- a. Observation confirmed at necropsy.
- b. Observation confirmed at necropsy; cut surface revealed firm, tan, lobular substance.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 13 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

DOSE GROUP III	MIDDLE DOSE	500 MG/KG/DAY
RAT #	DESCRIPTION	
11451	NO ADVERSE FINDINGS	
11452	NO ADVERSE FINDINGS	
11453	NO ADVERSE FINDINGS	
11454	NO ADVERSE FINDINGS	
11455	NO ADVERSE FINDINGS	
11456 DG (13- 21)	LOCALIZED ALOPECIA: LIMB (S) ^a	
11457 DG (11- 15)	NO ADVERSE FINDINGS	
11458 DG (16- 21)	SPARSE HAIR COAT	
DG (17- 21)	LOCALIZED ALOPECIA: LIMB (S) ^a	
11459	SPARSE HAIR COAT ^a	
11460 DG (15- 17)	NO ADVERSE FINDINGS	
11461 DG (15)	CHROMODACRYORRHEA	
DG (16)	SOFT OR LIQUID FECES	
11462 DG (16)	URINE-STAINED ABDOMINAL FUR	
11463 DG (16- 21)	URINE-STAINED ABDOMINAL FUR	
11464 DG (17)	NO ADVERSE FINDINGS	
DG (17)	SPARSE HAIR COAT ^a	
11465	EXCESS SALIVATION - SLIGHT	
11466	NO ADVERSE FINDINGS	
11467	NO ADVERSE FINDINGS	
11468	NO ADVERSE FINDINGS	
11469	NO ADVERSE FINDINGS	
11470	NO ADVERSE FINDINGS	
11471	NO ADVERSE FINDINGS	
11472	NO ADVERSE FINDINGS	
11473	NO ADVERSE FINDINGS	
11474	NO ADVERSE FINDINGS	
11475	NO ADVERSE FINDINGS	

DG = DAY OF PRESUMED GESTATION

a. Observation confirmed at necropsy.

PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 13 (PAGE 4): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #	DOSAGE GROUP IV	HIGH DOSAGE	1000 MG/KG/DAY
DESCRIPTION			
11476			NO ADVERSE FINDINGS
11477	DG (12- 21)	SPARSE HAIR COAT a	
	DG (21)	LEFT OF SIDE OF BACK: SCAB (0.5 CM IN DIAMETER) a	
11478		NO ADVERSE FINDINGS	
11479		NO ADVERSE FINDINGS	
11480		NO ADVERSE FINDINGS	
11481	DG (16)	RALES	
11482	DG (13- 21)	SPARSE HAIR COAT a	
11483		NO ADVERSE FINDINGS	
11484	DG (14)	EXCESS SALIVATION - MODERATE	
	DG (15)	EXCESS SALIVATION - EXTREME	
	DG (15- 16)	URINE-STAINED ABDOMINAL FOR	
	DG (16)	UNGROOMED COAT	
11485	DG (8- 21)	SPARSE HAIR COAT a	
11486	DG (17)	EXCESS SALIVATION - SLIGHT	
11487		NO ADVERSE FINDINGS	
11488	DG (17)	PTOSIS	
	DG (17)	EXCESS SALIVATION - EXTREME	
11489		NO ADVERSE FINDINGS	
11490		NO ADVERSE FINDINGS	
11491		NO ADVERSE FINDINGS	
11492	DG (19- 21)	SPARSE HAIR COAT a	
11493		NO ADVERSE FINDINGS	
11494		NO ADVERSE FINDINGS	
11495		NO ADVERSE FINDINGS	
11496	DG (9- 21)	SPARSE HAIR COAT a	
11497	DG (10- 21)	SPARSE HAIR COAT a	
11498		NO ADVERSE FINDINGS	
11499	DG (15)	EXCESS SALIVATION - SLIGHT	
11500		NO ADVERSE FINDINGS	

DG = DAY OF PRESUMED GESTATION

a. Observation confirmed at necropsy.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 14 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSE GROUP DOSEAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSES ADMINISTERED	OBSERVATIONS a
¹					
0 (Vehicle)	11401	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11402	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11403	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11404	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11405	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11406	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11407	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11408	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11409	DG 21	NP	11	ALL TISSUES APPEARED NORMAL.
	11410	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11411	DG 21	NP	11	ALL TISSUES APPEARED NORMAL.
	11412	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11413	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11414	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11415	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11416	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11417	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11418	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11419	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11420	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11421	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11422	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11423	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11424	DG 21	NP	11	ALL TISSUES APPEARED NORMAL.
	11425	DG 21	P	11	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION

P = PREGNANT NP = NOT PREGNANT

a. Refer to the individual clinical observations table (Table 13) for external observations confirmed at necropsy.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 14 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP DOSE/DOSE	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSES ADMINISTERED	OBSERVATIONS a
II					
250	11426	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11427	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11428	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11429	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11430	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11431	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11432	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11433	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11434	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11435	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11436	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11437	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11438	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11439	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11440	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11441	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11442	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11443	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11444	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11445	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11446	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11447	DG 21	NP	11	ALL TISSUES APPEARED NORMAL.
	11448	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11449	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11450	DG 21	P	11	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION

P = PREGNANT NP = NOT PREGNANT

a. Refer to the individual clinical observations table (Table 13) for external observations confirmed at necropsy.

TABLE 14 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP DOSEAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSES ADMINISTERED	OBSERVATIONS a
III 500	11451	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11452	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11453	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11454	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11455	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11456	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11457	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11458	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11459	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11460	DG 21	NP	11	ALL TISSUES APPEARED NORMAL.
	11461	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11462	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11463	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11464	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11465	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11466	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11467	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11468	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11469	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11470	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11471	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11472	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11473	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11474	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11475	DG 21	P	11	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION

P = PREGNANT NP = NOT PREGNANT

a. Refer to the individual clinical observations table (Table 13) for external observations confirmed at necropsy.

PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 14 (PAGE 4): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP DOSEAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSES ADMINISTERED	OBSERVATIONS a
IV 1000	11476	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11477	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11478	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11479	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11480	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11481	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11482	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11483	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11484	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11485	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11486	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11487	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11488	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11489	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11490	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11491	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11492	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11493	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11494	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11495	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11496	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11497	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11498	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11499	DG 21	P	11	ALL TISSUES APPEARED NORMAL.
	11500	DG 21	P	11	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION

P = PREGNANT NP = NOT PREGNANT

a. Refer to the individual clinical observations table (Table 13) for external observations confirmed at necropsy.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS
 TABLE 15 (PAGE 1): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	RAT #	VEHICLE CONTROL										0 (VEHICLE) MG/KG/DAY		
		DAY 0	7	8	9	10	11	12	13	14	15	16	17	18
	11401 P	218.	264.	261.	268.	273.	283.	290.	295.	300.	309.	319.	332.	342.
	11402 P	233.	281.	275.	274.	273.	283.	289.	291.	288.	300.	298.	307.	320.
	11403 P	240.	297.	292.	288.	299.	311.	315.	329.	332.	341.	351.	364.	380.
	11404 P	226.	260.	261.	259.	263.	270.	277.	274.	283.	286.	302.	313.	332.
	11405 P	236.	275.	274.	278.	289.	297.	304.	313.	310.	304.	309.	331.	344.
	11406 P	225.	262.	260.	270.	269.	278.	277.	284.	284.	302.	315.	317.	336.
	11407 P	234.	286.	294.	291.	294.	292.	297.	292.	291.	308.	322.	327.	346.
	11408 P	231.	276.	277.	279.	280.	285.	282.	290.	291.	297.	309.	316.	324.
	11409 NP	240.	295.	300.	302.	310.	314.	318.	315.	306.	309.	316.	315.	308.
	11410 P	229.	275.	272.	278.	280.	291.	296.	294.	298.	307.	324.	341.	352.
	11411 NP	230.	248.	252.	251.	253.	253.	252.	259.	260.	263.	258.	266.	262.
	11412 P	223.	274.	274.	276.	278.	290.	296.	305.	313.	320.	333.	350.	367.
	11413 P	233.	282.	281.	275.	275.	288.	292.	300.	307.	311.	324.	337.	350.
	11414 P	232.	264.	264.	262.	271.	275.	274.	273.	273.	284.	304.	323.	337.
	11415 P	226.	272.	274.	277.	278.	288.	294.	295.	311.	322.	337.	350.	371.
	11416 P	223.	257.	254.	251.	260.	269.	276.	280.	276.	279.	289.	303.	316.
	11417 P	238.	275.	266.	271.	270.	276.	284.	285.	292.	302.	310.	324.	356.
	11418 P	228.	263.	258.	258.	258.	263.	266.	275.	281.	280.	295.	319.	341.
	11419 P	229.	273.	269.	272.	282.	293.	292.	296.	305.	315.	326.	341.	358.
	11420 P	235.	287.	288.	288.	284.	292.	295.	308.	317.	323.	338.	348.	367.
	11421 P	241.	285.	273.	273.	290.	302.	306.	314.	333.	350.	367.	390.	371.
	11422 P	234.	268.	260.	259.	265.	268.	268.	282.	282.	286.	296.	300.	310.
	11423 P	221.	259.	261.	260.	261.	269.	275.	282.	285.	294.	310.	327.	340.
	11424 NP	222.	242.	238.	237.	239.	242.	244.	242.	248.	249.	248.	252.	252.
	11425 P	243.	279.	269.	271.	267.	271.	278.	290.	297.	310.	322.	343.	362.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAY OF PRESUMED GESTATION
 ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TIE00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 15 (PAGE 2): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 19	20	21	VEHICLE CONTROL		0 (VEHICLE) MG/KG/DAY
				RAT #	DOSAGE GROUP I	
11401 P	356.	366.	393.			
11402 P	331.	338.	364.			
11403 P	407.	428.	461.			
11404 P	341.	360.	381.			
11405 P	360.	375.	408.			
11406 P	354.	369.	410.			
11407 P	370.	394.	423.			
11408 P	339.	350.	379.			
11409 NP	318.	316.	324.			
11410 P	366.	386.	408.			
11411 NP	265.	266.	265.			
11412 P	378.	396.	414.			
11413 P	361.	378.	392.			
11414 P	352.	368.	395.			
11415 P	383.	409.	437.			
11416 P	321.	343.	365.			
11417 P	374.	393.	426.			
11418 P	330.	341.	362.			
11419 P	377.	391.	424.			
11420 P	384.	406.	438.			
11421 P	408.	414.	451.			
11422 P	336.	348.	379.			
11423 P	358.	376.	400.			
11424 NP	256.	254.	254.			
11425 P	376.	392.	416.			

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAY OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 15 (PAGE 3): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	RAT #	DOSE GROUP I						DOSE GROUP II						250 MG/KG/DAY					
		DAY 0	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
	11426 P	227.	280.	284.	290.	284.	292.	302.	309.	311.	331.	340.	330.	330.	330.	330.	330.	330.	
	11427 P	221.	280.	280.	284.	280.	296.	304.	295.	294.	287.	288.	320.	320.	320.	320.	320.	320.	
	11428 P	232.	263.	267.	268.	267.	276.	288.	288.	301.	302.	309.	326.	326.	326.	326.	326.	326.	
	11429 P	226.	263.	260.	247.	252.	262.	271.	272.	272.	279.	286.	296.	296.	296.	296.	296.	296.	
	11430 P	233.	282.	282.	286.	285.	298.	304.	311.	320.	322.	330.	344.	344.	344.	344.	344.	344.	
	11431 P	229.	276.	274.	273.	270.	280.	285.	278.	284.	305.	322.	341.	341.	341.	341.	341.	341.	
	11432 P	234.	271.	271.	280.	288.	292.	298.	306.	312.	318.	331.	343.	343.	343.	343.	343.	343.	
	11433 P	235.	271.	277.	276.	280.	286.	294.	296.	302.	302.	310.	316.	316.	316.	316.	316.	316.	
	11434 P	226.	264.	262.	258.	263.	278.	288.	287.	296.	301.	306.	322.	322.	322.	322.	322.	322.	
	11435 P	235.	281.	282.	289.	290.	302.	305.	315.	322.	325.	339.	352.	352.	352.	352.	352.	352.	
	11436 P	243.	301.	297.	304.	313.	321.	330.	343.	352.	365.	382.	400.	400.	400.	400.	400.	400.	
	11437 P	230.	277.	273.	276.	282.	293.	292.	298.	308.	321.	332.	357.	357.	357.	357.	357.	357.	
	11438 P	240.	282.	276.	276.	284.	292.	298.	301.	310.	320.	335.	346.	346.	346.	346.	346.	346.	
	11439 P	223.	269.	268.	273.	279.	282.	289.	295.	300.	310.	319.	333.	333.	333.	333.	333.	333.	
	11440 P	241.	283.	289.	286.	289.	298.	308.	316.	323.	331.	345.	359.	359.	359.	359.	359.	359.	
	11441 P	225.	252.	253.	261.	267.	270.	279.	283.	288.	307.	318.	336.	336.	336.	336.	336.	336.	
	11442 P	240.	275.	273.	272.	275.	277.	285.	289.	297.	309.	318.	329.	329.	329.	329.	329.	329.	
	11443 P	222.	263.	267.	272.	274.	278.	289.	295.	295.	304.	313.	324.	324.	324.	324.	324.	324.	
	11444 P	230.	280.	281.	285.	300.	311.	315.	321.	328.	344.	355.	377.	377.	377.	377.	377.	377.	
	11445 P	218.	262.	263.	268.	275.	280.	288.	289.	298.	301.	311.	325.	325.	325.	325.	325.	325.	
	11446 P	237.	272.	271.	278.	282.	288.	294.	301.	302.	310.	316.	334.	334.	334.	334.	334.	334.	
	11447 P	228.	262.	266.	267.	268.	279.	289.	282.	295.	307.	319.	332.	332.	332.	332.	332.	332.	
	11448 NP	240.	270.	270.	271.	271.	271.	269.	276.	267.	271.	275.	275.	275.	275.	275.	275.	275.	
	11449 P	224.	265.	269.	270.	280.	286.	287.	293.	301.	307.	318.	327.	327.	327.	327.	327.	327.	
	11450 P	233.	267.	250.	267.	276.	274.	282.	285.	289.	287.	294.	310.	310.	310.	310.	310.	310.	

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DRY = DAY OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 15 (PAGE 4): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 19	20		21	LOW DOSAGE GROUP II	250 MG/KG/DAY
		RAT #	DOSAGE			
		11426 P	363.	372.	393.	
		11427 P	339.	359.	397.	
		11428 P	347.	366.	392.	
		11429 P	334.	353.	385.	
		11430 P	371.	386.	404.	
		11431 P	371.	381.	404.	
		11432 P	369.	387.	403.	
		11433 P	343.	355.	383.	
		11434 P	344.	363.	386.	
		11435 P	384.	403.	424.	
		11436 P	417.	444.	473.	
		11437 P	369.	388.	424.	
		11438 P	381.	385.	420.	
		11439 P	365.	370.	396.	
		11440 P	382.	394.	412.	
		11441 P	351.	362.	388.	
		11442 P	349.	369.	390.	
		11443 P	343.	354.	378.	
		11444 P	413.	431.	458.	
		11445 P	354.	370.	404.	
		11446 P	356.	376.	398.	
		11447 P	358.	371.	390.	
		11448 NP	266.	274.	283.	
		11449 P	364.	376.	398.	
		11450 P	350.	357.	383.	

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAY OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS
 TABLE 15 (PAGE 5): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY	0	7	8	9	10	11	12	13	14	15	16	17	18	MIDDLE DOSE		500 MG/KG/DAY	
															RAT #	DOSE	GROUP	III
11451 P	225.	262.	268.	270.	272.	275.	283.	285.	292.	295.	301.	307.	318.	333.				
11452 P	220.	252.	249.	247.	253.	260.	268.	266.	276.	281.	289.	299.	315.					
11453 P	233.	284.	285.	292.	301.	322.	322.	322.	331.	345.	358.	358.	380.	398.				
11454 P	228.	271.	273.	268.	279.	292.	294.	300.	310.	320.	336.	336.	349.	359.				
11455 P	226.	286.	290.	289.	296.	308.	309.	309.	321.	325.	333.	333.	348.	366.				
11456 P	225.	262.	255.	253.	266.	278.	279.	287.	294.	301.	313.	325.	325.	339.				
11457 P	243.	293.	275.	280.	283.	299.	300.	306.	308.	328.	336.	336.	355.	369.				
11458 P	230.	270.	268.	268.	273.	284.	292.	300.	309.	316.	321.	321.	349.	349.				
11459 P	240.	292.	296.	303.	311.	321.	321.	328.	325.	333.	348.	348.	359.	372.				
11460 NP	221.	251.	246.	249.	253.	253.	261.	260.	259.	261.	263.	263.	264.	266.				
11461 P	233.	288.	286.	292.	302.	312.	324.	327.	335.	341.	350.	350.	368.	387.				
11462 P	223.	257.	256.	261.	267.	275.	275.	275.	284.	286.	292.	292.	313.	332.				
11463 P	240.	291.	284.	277.	280.	290.	298.	298.	300.	309.	323.	323.	345.	365.				
11464 P	227.	277.	274.	281.	280.	286.	297.	297.	298.	303.	312.	312.	333.	345.				
11465 P	232.	279.	281.	284.	291.	295.	305.	305.	310.	316.	327.	327.	360.	374.				
11466 P	243.	281.	279.	285.	292.	292.	292.	307.	314.	324.	333.	333.	348.	367.				
11467 P	239.	271.	276.	273.	276.	282.	290.	298.	300.	300.	313.	313.	326.	331.				
11468 P	222.	263.	259.	258.	266.	274.	275.	284.	294.	294.	312.	312.	333.	349.				
11469 P	229.	277.	274.	276.	279.	291.	292.	298.	310.	317.	328.	328.	345.	365.				
11470 P	235.	271.	268.	273.	279.	285.	287.	296.	304.	318.	334.	334.	345.	366.				
11471 P	232.	260.	256.	254.	250.	254.	261.	272.	272.	278.	291.	291.	306.	320.				
11472 P	226.	241.	246.	241.	251.	257.	259.	260.	267.	273.	278.	278.	284.	293.				
11473 P	226.	272.	272.	275.	281.	284.	285.	293.	298.	312.	320.	320.	335.	361.				
11474 P	230.	257.	262.	260.	275.	270.	274.	279.	281.	299.	316.	316.	316.	332.				
11475 P	237.	257.	264.	269.	278.	278.	288.	292.	294.	300.	314.	314.	322.	340.				

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAY OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TIE00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 15 (PAGE 6): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 19	20	21	MIDDLE DOSEAGE	
				RAT #	DOSEAGE GROUP III
				11451 P	348.
				11452 P	333.
				11453 P	419.
				11454 P	389.
				11455 P	385.
				11456 P	357.
				11457 P	394.
				11458 P	367.
				11459 P	387.
				11460 NP	268.
				11461 P	400.
				11462 P	347.
				11463 P	385.
				11464 P	362.
				11465 P	391.
				11466 P	384.
				11467 P	357.
				11468 P	366.
				11469 P	380.
				11470 P	384.
				11471 P	333.
				11472 P	306.
				11473 P	375.
				11474 P	337.
				11475 P	364.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAY OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 15 (PAGE 7): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY	0	7	8	9	10	11	12	13	14	15	16	17	18	HIGH DOSAGE		1000 MG/KG/DAY
															DOORAGE GROUP	IV	
11476 P	226.	273.	267.	269.	280.	289.	292.	302.	313.	316.	341.	353.	367.				
11477 P	227.	264.	262.	260.	259.	275.	272.	282.	284.	290.	298.	314.	326.				
11478 P	224.	257.	254.	260.	263.	274.	282.	282.	293.	292.	306.	319.	335.				
11479 P	229.	277.	275.	276.	282.	288.	302.	308.	313.	329.	333.	352.	362.				
11480 P	242.	282.	283.	280.	288.	290.	296.	299.	306.	312.	324.	344.	356.				
11481 P	238.	266.	249.	261.	271.	272.	276.	276.	280.	290.	297.	310.	329.				
11482 P	222.	269.	279.	281.	282.	288.	293.	304.	314.	321.	321.	330.	350.				
11483 P	232.	262.	262.	249.	252.	259.	278.	286.	287.	295.	295.	304.	318.				
11484 P	226.	267.	268.	267.	276.	285.	292.	294.	290.	292.	292.	313.	324.				
11485 P	220.	273.	257.	252.	268.	276.	277.	277.	283.	288.	295.	308.	313.				
11486 P	244.	283.	292.	289.	292.	296.	299.	305.	311.	315.	335.	335.	338.				
11487 P	241.	287.	280.	270.	286.	295.	295.	308.	305.	310.	348.	348.	363.				
11488 P	230.	272.	271.	255.	243.	233.	225.	215.	215.	241.	258.	272.	283.				
11489 P	227.	254.	254.	258.	258.	266.	274.	280.	280.	284.	294.	312.	319.				
11490 P	233.	283.	277.	272.	280.	297.	303.	308.	315.	329.	337.	358.	369.				
11491 P	240.	290.	273.	267.	272.	282.	295.	307.	308.	322.	327.	347.	364.				
11492 P	223.	261.	259.	263.	263.	273.	281.	290.	290.	300.	308.	317.	335.				
11493 P	235.	268.	260.	264.	268.	275.	280.	282.	295.	304.	329.	338.	338.				
11494 P	218.	248.	241.	243.	249.	259.	260.	269.	276.	277.	289.	300.	315.				
11495 P	225.	265.	257.	254.	255.	249.	261.	275.	275.	272.	273.	290.	303.				
11496 P	234.	272.	267.	264.	272.	278.	286.	293.	298.	298.	312.	323.	343.				
11497 P	233.	282.	277.	280.	287.	290.	299.	308.	306.	329.	344.	361.	361.				
11498 P	237.	274.	270.	275.	279.	287.	292.	297.	304.	321.	321.	340.	340.				
11499 P	231.	270.	259.	257.	267.	278.	287.	290.	294.	304.	321.	321.	340.				
11500 P	229.	262.	263.	268.	272.	272.	272.	271.	279.	286.	294.	308.	328.				

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAY OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 15 (PAGE 8): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	RAT #	DAY 19	DAY 20	DAY 21	HIGH DOSAGE		1000 MG/KG/DAY
					DOSEAGE	GROUP IV	
	11476 P	361.	372.	403.			
	11477 P	333.	356.	378.			
	11478 P	353.	370.	382.			
	11479 P	370.	385.	418.			
	11480 P	377.	403.	436.			
	11481 P	342.	359.	384.			
	11482 P	373.	394.	418.			
	11483 P	344.	360.	407.			
	11484 P	349.	357.	378.			
	11485 P	347.	362.	389.			
	11486 P	362.	386.	405.			
	11487 P	382.	404.	438.			
	11488 P	310.	317.	344.			
	11489 P	326.	334.	361.			
	11490 P	388.	391.	427.			
	11491 P	384.	403.	430.			
	11492 P	355.	380.	413.			
	11493 P	358.	381.	412.			
	11494 P	322.	336.	354.			
	11495 P	343.	355.	382.			
	11496 P	369.	387.	406.			
	11497 P	375.	404.	430.			
	11498 P	330.	338.	366.			
	11499 P	353.	371.	393.			
	11500 P	345.	360.	392.			

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAY OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS
 TABLE 16 (PAGE 1): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

RAT #	PREGNANCY STATUS	DAYS	0 - 7 7 - 10 10 - 12 12 - 15 15 - 18 18 - 21						VEHICLE CONTROL	0 (VEHICLE) MG/KG/DAY
			DOSE GROUP I							
11401 P	P	171.	54.	42.	62.	68.	72.			
11402 P	P	167.	40.	38.	52.	62.	88.			
11403 P	P	191.	51.	44.	58.	71.	104.			
11404 P	P	193.	45.	31.	45.	54.	66.			
11405 P	P	174.	57.	39.	45.	55.	93.			
11406 P	P	171.	51.	35.	63.	63.	86.			
11407 P	P	197.	72.	35.	45.	64.	101.			
11408 P	P	171.	53.	24.	51.	61.	84.			
11409 NP		180.	76.	41.	50.	43.	64.			
11410 P	P	167.	54.	39.	49.	73.	80.			
11411 NP		157.	58.	25.	53.	47.	61.			
11412 P	P	173.	55.	40.	64.	70.	79.			
11413 P	P	172.	46.	34.	58.	62.	72.			
11414 P	P	157.	48.	30.	39.	71.	76.			
11415 P	P	150.	51.	34.	59.	73.	81.			
11416 P	P	149.	37.	32.	45.	51.	62.			
11417 P	P	171.	41.	31.	51.	66.	94.			
11418 P	P	158.	43.	26.	48.	132.a	61.			
11419 P	P	160.	56.	43.	62.	20.	96.			
11420 P	P	185.	45.	42.	63.	46.	83.			
11421 P	P	182.	48.	41.	52.	86.	87.			
11422 P	P	149.	26.	21.	49.	43.	76.			
11423 P	P	155.	49.	35.	50.	66.	82.			
11424 NP		142.	35.	30.	41.	45.	53.			
11425 P	P	177.	37.	29.	59.	88.	89.			

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAYS OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Value appeared incorrectly recorded and was excluded from summarization and statistical analyses.

PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 16 (PAGE 2): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS	250 MG/KG/DAY					
		0 - 7	7 - 10	10 - 12	12 - 15	15 - 18	18 - 21
RAT #	DOSEAGE GROUP II	LOW DOSAGE					
11426 P	185.	59.	36.	a	55.	80.	
11427 P	179.	53.	37.	34.	59.	88.	
11428 P	145.	41.	28.	56.	72.	89.	
11429 P	156.	35.	40.	a	61.	96.	
11430 P	176.	53.	40.	59.	62.	75.	
11431 P	168.	35.	28.	42.	78.	91.	
11432 P	165.	52.	32.	56.	59.	68.	
11433 P	176.	61.	43.	74.	69.	80.	
11434 P	160.	37.	37.	56.	57.	69.	
11435 P	a	58.	37.	73.	66.	79.	
11436 P	212.	63.	45.	81.	91.	96.	
11437 P	179.	54.	34.	58.	69.	87.	
11438 P	163.	50.	36.	60.	72.	74.	
11439 P	167.	48.	33.	51.	68.	70.	
11440 P	172.	55.	48.	63.	86.	96.	
11441 P	145.	41.	31.	52.	68.	66.	
11442 P	162.	37.	33.	56.	62.	67.	
11443 P	148.	55.	32.	59.	60.	76.	
11444 P	166.	68.	49.	66.	87.	90.	
11445 P	167.	56.	44.	62.	69.	83.	
11446 P	147.	49.	39.	49.	59.	72.	
11447 P	149.	48.	40.	57.	69.	77.	
11448 NP	155.	42.	27.	b	35.	50.	
11449 P	162.	56.	38.	54.	60.	72.	
11450 P	169.	41.	37.	49.	71.	89.	

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAYS = DAYS OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Spilled feed precluded the calculation of this value.

b. Value could not be calculated.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS
 TABLE 16 (PAGE 3): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

RAT #	PREGNANCY STATUS DRAWS	0 - 7	7 - 10	10 - 12	12 - 15	15 - 18	18 - 21	MIDDLE DOSAGE		500 MG/KG/DAY	
								DOSE GROUP III	MIDDLE DOSAGE	DOSE GROUP III	MIDDLE DOSAGE
11451 P	166.	56.	32.	50.	61.	80.					
11452 P	143.	36.	26.	46.	46.	69.					
11453 P	184.	60.	42.	67.	77.	91.					
11454 P	116.	42.	41.	51.	63.	98.					
11455 P	182.	52.	37.	55.	74.	89.					
11456 P	152.	35.	34.	53.	61.	82.					
11457 P	178.	40.	33.	67.	65.	100.					
11458 P	186.	43.	37.	57.	47.	84.					
11459 P	203.	70.	35.	61.	73.	100.					
11460 NP	149.	42.	30.	40.	41.	58.					
11461 P	199.	a	46.	54.	70.	86.					
11462 P	b	56.	33.	53.	68.	83.					
11463 P	183.	33.	30.	45.	63.	96.					
11464 P	178.	57.	33.	48.	58.	90.					
11465 P	179.	65.	46.	a	78.	86.					
11466 P	163.	49.	39.	64.	62.	73.					
11467 P	171.	55.	29.	54.	56.	78.					
11468 P	164.	48.	30.	60.	75.	83.					
11469 P	183.	47.	35.	62.	80.	92.					
11470 P	143.	50.	40.	62.	73.	96.					
11471 P	145.	39.	26.	37.	63.	79.					
11472 P	131.	37.	25.	43.	39.	69.					
11473 P	161.	78.	34.	55.	83.	89.					
11474 P	146.	41.	28.	45.	48.	55.					
11475 P	146.	49.	33.	46.	48.	95.					

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAYS OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Value was presumed to be associated with spillage and was excluded from summarization and statistical analyses.

b. Spilled feed precluded the calculation of this value.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 16 (PAGE 4): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	0 - 7	7 - 10	10 - 12	12 - 15	15 - 18	18 - 21	HIGH DOSAGE	1000 MG/KG/DAY
RAT #	DOSE GROUP IV							
11476 P	183.	49.	32.	56.	51.	66.		
11477 P	155.	36.	24.	46.	54.	77.		
11478 P	154.	39.	33.	55.	65.	86.		
11479 P	162.	44.	29.	60.	53.	78.		
11480 P	181.	37.	28.	40.	59.	94.		
11481 P	157.	41.	27.	56.	60.	82.		
11482 P	184.	55.	31.	73.	70.	99.		
11483 P	140.	22.	20.	50.	47.	73.		
11484 P	166.	41.	33.	31.	56.	90.		
11485 P	154.	33.	31.	45.	59.	92.		
11486 P	188.	44.	26.	44.	36.	76.		
11487 P	175.	31.	27.	42.	63.	91.		
11488 P	161.	18.	1.	38.	61.	75.		
11489 P	149.	37.	29.	48.	53.	58.		
11490 P	189.	38.	38.	65.	76.	79.		
11491 P	178.	23.	40.	41.	64.	90.		
11492 P	145.	40.	38.	50.	54.	97.		
11493 P	146.	35.	32.	49.	57.	92.		
11494 P	147.	27.	42.	39.	55.	71.		
11495 P	150.	38.	24.	41.	64.	86.		
11496 P	156.	24.	36.	43.	56.	87.		
11497 P	168.	47.	36.	57.	63.	95.		
11498 P	169.	50.	33.	48.	52.	79.		
11499 P	165.	32.	43.	46.	55.	92.		
11500 P	152.	51.	22.	39.	72.	85.		

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)

DAY = DAYS OF PREGNANCY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 17 (PAGE 1): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

		VEHICLE CONTROL										0 (VEHICLE) MG/KG/DAY							
		VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES		CORPORA LUTEA			
DOSAGE GROUP I		SEX	RIGHT LEFT	HORN	RIGHT LEFT	HORN	RIGHT LEFT	HORN	RIGHT LEFT	HORN	RIGHT LEFT	HORN	RIGHT LEFT	HORN	RIGHT LEFT	OVARY	TOTAL		
RAT #	M F																		
11401	6 6	5	7	12	0	0	0	2	0	0	0	0	5	9	14	5	10	15	
11402	2 5	5	2	7	0	0	0	0	0	0	0	0	5	2	7	5	2	7	
11403	8 9	5	12	17	0	0	0	0	0	0	0	0	5	12	17	6	12	18	
11404	7 7	4	10	14	0	0	1	0	1	0	0	0	5	10	15	5	10	15	
11405	7 8	8	7	15	0	0	0	1	1	1	0	1	9	8	17	10	8	18	
11406	7 7	6	8	14	0	0	0	0	0	0	0	0	6	8	14	6	8	14	
11407	9 6	8	7	15	0	0	0	1	0	0	0	0	9	7	16	10	8	18	
11408	6 4	1	9	10	0	0	0	2	0	0	0	0	3	9	12	3	9	12	
11409	NOT PREGNANT																		
11410	7 7	7	7	14	0	0	0	1	0	0	0	0	0	8	7	15	8	8	16
11411	NOT PREGNANT																		
11412	8 7	9	6	15	0	0	0	0	0	0	0	0	0	9	6	15	9	6	15
11413	5 6	7	4	11	0	0	0	0	1	0	0	0	0	8	4	12	8	5	13
11414	5 10	7	8	15	0	0	0	0	0	0	0	0	0	7	8	15	7	8	15
11415	8 7	11	4	15	0	0	0	0	0	0	0	0	0	11	4	15	11	4	15
11416	5 8	8	5	13	0	0	0	0	0	0	0	0	0	8	5	13	8	5	13
11417	5 9	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	8	14
11418	8 6	5	9	14	0	0	0	0	0	0	0	0	0	5	9	14	7	10	17
11419	7 6	5	8	13	0	0	0	0	1	0	0	0	0	5	9	14	5	9	14
11420	5 9	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	8	14
11421	8 7	6	9	15	0	0	0	1	0	0	0	0	6	10	16	6	10	16	
11422	6 5	8	3	11	0	0	0	1	0	0	0	0	9	3	12	9	3	12	
11423	3 11	7	14	0	0	0	0	0	0	0	0	0	7	7	14	7	7	14	
11424	NOT PREGNANT																		
11425	8 5	8	5	13	0	0	0	0	0	0	0	0	0	8	5	13	9	7	16

M = MALE F = FEMALE
 PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 17 (PAGE 2): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

RAT #	DOSE GROUP II		LOW DOSAGE						250 MG/KG/DAY										
	VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA			
	SEX	M	F	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	
11426	5	7	7	5	12	0	0	0	1	0	0	0	5	13	9	7	16		
11427	3	6	3	6	9	0	0	0	0	0	0	0	3	6	9	3	6	9	
11428	8	5	9	4	13	0	0	1	1	0	0	0	10	5	15	10	5	15	
11429	7	4	8	3	11	0	0	0	1	1	0	0	0	8	4	12	9	4	13
11430	4	9	7	6	13	0	0	0	0	0	0	0	0	7	6	13	7	6	13
11431	1	11	5	7	12	0	0	0	0	0	0	0	0	5	7	12	5	7	12
11432	4	10	9	5	14	0	0	0	1	1	0	0	0	10	6	16	12	8	20
11433	6	3	9	0	9	0	0	0	0	0	0	0	0	9	0	9	9	7	16
11434	6	5	8	3	11	0	0	0	1	1	0	0	0	9	4	13	9	5	14
11435	7	9	8	8	16	0	0	1	0	1	0	0	0	9	8	17	9	9	18
11436	7	7	6	8	14	0	0	0	0	0	0	0	0	6	8	14	6	8	14
11437	6	9	8	7	15	0	0	0	0	0	0	0	0	8	7	15	8	7	15
11438	8	7	9	6	15	0	0	0	0	2	0	0	0	9	8	17	9	9	18
11439	3	10	3	13	0	0	0	0	1	0	1	0	0	11	3	14	11	6	17
11440	7	0	4	3	7	0	0	0	0	0	0	0	0	4	3	7	5	4	9
11441	9	6	7	8	15	0	0	0	0	0	0	0	0	7	8	15	7	8	15
11442	8	6	10	4	14	0	0	0	0	0	0	0	0	10	4	14	12	4	16
11443	5	9	8	6	14	0	0	0	2	0	2	0	0	10	6	16	11	6	17
11444	10	8	10	8	18	0	0	0	1	1	0	0	0	11	9	20	11	9	20
11445	8	7	7	8	15	0	0	0	0	0	0	0	0	7	8	15	7	8	15
11446	8	5	8	5	13	0	0	0	0	0	0	0	0	5	13	8	5	13	
11447	4	8	6	6	12	0	0	0	2	2	0	0	0	8	14	6	9	15	
11448	NOT PREGNANT																		
11449	5	9	5	9	14	0	0	0	0	0	0	0	0	5	9	14	5	9	14
11450	6	6	6	6	12	0	0	0	2	0	0	0	0	6	14	8	6	6	14

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 17 (PAGE 3): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

RAT #	SEX M F	DOSE GROUP III MIDDLE DOSAGE	500 MG/KG/DAY																	
			Viable Fetusess			Dead Fetusess			Early Resorptions			Late Resorptions			Implantation Sites			Corpora Lutea		
			Right	Horn	Total	Right	Horn	Total	Right	Horn	Total	Right	Horn	Total	Right	Horn	Total	Right	Left	Ovary
11451	2	10	6	6	12	0	0	0	0	0	0	0	0	0	6	6	12	8	8	16
11452	7	6	6	7	13	0	0	0	1	0	1	0	0	0	6	8	14	6	8	14
11453	11	8	9	10	19	0	0	0	0	0	0	0	0	0	9	10	19	9	10	19
11454	10	7	9	8	17	0	0	0	0	0	0	0	0	0	8	8	17	9	8	17
11455	5	8	8	5	13	0	0	0	0	1	1	0	0	0	6	6	14	8	6	14
11456	5	8	7	6	13	0	0	0	0	1	1	0	0	0	7	7	14	7	7	14
11457	8	9	7	10	17	0	0	0	0	0	0	0	0	0	7	7	14	7	7	14
11458	12	5	9	8	17	0	0	0	0	0	0	0	0	0	9	8	17	9	8	17
11459	7	6	6	7	13	0	0	0	1	0	1	0	0	0	7	7	14	7	7	14
11460	NOT PREGNANT																			
11461	7	8	6	9	15	0	0	0	1	0	1	0	0	0	7	9	16	7	10	17
11462	8	5	5	8	13	0	0	0	1	0	1	0	0	0	6	8	14	6	8	14
11463	7	9	10	6	16	0	0	0	1	0	1	0	0	0	11	6	17	11	7	18
11464	8	6	5	9	14	0	0	0	0	0	0	0	0	0	5	9	14	6	9	15
11465	9	6	10	5	15	0	0	0	0	0	0	0	0	0	10	5	15	11	5	16
11466	7	9	7	16	0	0	0	0	0	0	0	0	0	0	9	7	16	10	7	17
11467	7	5	9	14	0	0	0	1	0	1	0	0	0	0	6	9	15	7	10	17
11468	9	3	6	6	12	0	0	0	2	0	2	0	0	0	6	8	14	6	9	15
11469	7	8	9	6	15	0	0	0	1	0	1	0	0	0	10	6	16	10	6	16
11470	6	10	8	16	0	0	0	0	0	0	0	0	0	0	8	8	16	9	10	19
11471	7	6	9	4	13	0	0	0	1	0	1	0	0	0	10	4	14	6	20	
11472	7	4	7	4	11	0	0	0	1	0	1	0	0	0	8	4	12	8	4	12
11473	7	10	10	7	17	0	0	0	0	0	0	0	0	0	10	7	17	12	10	22
11474	8	6	7	7	14	0	0	0	0	0	0	0	0	0	7	7	14	7	7	14
11475	8	7	9	6	15	0	0	0	1	0	1	0	0	0	10	6	16	10	6	16

M = MALE F = FEMALE
 PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 17 (PAGE 4): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

DOSE GROUP IV				HIGH DOSAGE												1000 MG/KG/DAY					
RAT #	M	F	SEX	Viable Fetuses			Dead Fetuses			Early Resorptions			Late Resorptions			Implantation Sites			Corpora Lutea		
				HORN	RIGHT	LEFT	HORN	RIGHT	LEFT	HORN	RIGHT	LEFT	HORN	RIGHT	LEFT	HORN	RIGHT	LEFT	Ovary	Total	
11476	11	5	M	5	11	16	0	0	0	1	0	0	0	0	0	6	11	17	6	11	17
11477	8	6	M	8	6	14	0	0	0	0	0	0	0	0	0	8	6	14	9	6	15
11478	9	6	M	5	10	15	0	0	0	0	0	0	0	0	0	5	10	15	6	10	16
11479	7	6	M	6	7	13	0	0	0	0	0	0	0	0	0	6	7	13	6	8	14
11480	9	9	M	11	7	18	0	0	0	0	0	0	0	0	0	11	7	18	12	8	20
11481	3	9	M	8	4	12	0	0	0	0	1	0	0	0	0	5	13	8	6	14	14
11482	5	8	M	7	6	13	0	0	0	1	0	1	0	0	0	8	6	14	8	6	14
11483	13	3	M	8	8	16	0	0	0	0	1	1	0	0	0	8	9	17	8	9	17
11484	8	3	M	4	7	11	0	0	0	0	0	0	0	0	0	4	7	11	4	7	11
11485	5	9	M	8	6	14	0	0	0	0	0	0	0	0	0	8	6	14	8	6	14
11486	14	3	M	8	9	17	0	0	0	0	0	0	0	0	0	8	9	17	8	9	17
11487	10	6	M	10	6	16	0	0	0	0	0	0	0	0	0	6	10	16	6	10	16
11488	7	6	M	7	6	13	0	0	0	0	1	1	0	0	0	7	14	10	7	17	17
11489	4	8	M	8	12	0	0	0	0	0	0	0	0	0	0	4	8	12	6	8	14
11490	8	8	M	9	7	16	0	0	0	0	0	0	0	0	0	9	7	16	9	7	16
11491	6	11	M	12	5	17	0	0	0	0	0	0	0	0	0	12	5	17	12	5	17
11492	8	6	M	7	7	14	0	0	0	0	0	0	0	0	0	7	7	14	7	8	15
11493	5	11	M	10	6	16	0	0	0	0	0	0	0	0	0	10	6	16	15	8	23
11494	7	7	M	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	8	14
11495	8	6	M	7	14	0	0	0	0	0	0	0	0	0	0	7	14	8	8	16	16
11496	11	5	M	9	7	16	0	0	0	0	0	0	0	0	0	9	7	16	9	7	16
11497	10	7	M	11	6	17	0	0	0	0	0	0	0	0	0	11	6	17	11	7	18
11498	2	5	M	1	6	7	0	0	0	2	4	6	0	0	0	3	10	13	4	11	15
11499	9	4	M	8	5	13	0	0	0	1	0	0	0	0	0	9	5	14	9	5	14
11500	5	9	M	8	6	14	0	0	0	0	0	0	0	0	0	8	6	14	8	8	16

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 18 (PAGE 1): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

RAT #	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			0 (VEHICLE) MG/KG/DAY		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL	a	TOTAL	CONCEPTUSES RESORBED
11401	6	6	12	5.77	5.36	5.56	14	2	14.3
11402	2	5	7	5.75	5.77	5.76	7	0	0.0
11403	8	9	17	5.58	5.39	5.48	17	0	0.0
11404	7	7	14	5.76	5.51	5.64	15	1	6.7
11405	7	8	15	5.36	5.18	5.26	17	2	11.8
11406	7	7	14	5.93	5.42	5.67	14	0	0.0
11407	9	6	15	5.48	5.26	5.40	16	1	6.2
11408	6	4	10	5.83	5.58	5.73	12	2	16.7
11409	NOT PREGNANT								
11410	7	7	14	5.85	5.72	5.78	15	1	6.7
11411	NOT PREGNANT								
11412	8	7	15	5.31	5.13	5.22	15	0	0.0
11413	5	6	11	5.57	5.44	5.50	12	1	8.3
11414	5	10	15	5.44	5.05	5.18	15	0	0.0
11415	8	7	15	5.81	5.47	5.65	15	0	0.0
11416	5	8	13	5.06	4.94	4.99	13	0	0.0
11417	5	9	14	5.72	5.42	5.53	14	0	0.0
11418	8	6	14	5.14	4.76	4.97	14	0	0.0
11419	7	6	13	5.55	5.10	5.34	14	1	7.1
11420	5	9	14	5.85	5.72	5.77	14	0	0.0
11421	8	7	15	5.71	5.59	5.66	16	1	6.2
11422	6	5	11	6.22	5.58	5.93	12	1	8.3
11423	3	11	14	5.36	5.09	5.15	14	0	0.0
11424	NOT PREGNANT								
11425	8	5	13	5.82	5.85	5.83	13	0	0.0

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 18 (PAGE 2): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

RAT #	DOSE GROUP II			LOW DOSAGE			250 MG/KG/DAY			
	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			CONCEPSES			
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	TOTAL	RESORBED	N	%
11426	5	7	12	5.45	5.06	5.22	13	1	1	7.7
11427	3	6	9	6.07	5.70	5.82	9	0	0	0.0
11428	8	5	13	5.56	5.32	5.47	15	2	1	13.3
11429	7	4	11	6.00	5.85	5.95	12	1	1	8.3
11430	4	9	13	6.16	5.84	5.94	13	0	0	0.0
11431	1	11	12	6.01	5.32	5.38	12	0	0	0.0
11432	4	10	14	5.44	5.17	5.24	16	2	1	12.5
11433	6	3	9	5.90	5.61	5.80	9	0	0	0.0
11434	6	5	11	5.88	5.57	5.74	13	2	1	15.4
11435	7	9	16	5.74	5.51	5.61	17	1	1	5.9
11436	7	7	14	6.08	5.64	5.86	14	0	0	0.0
11437	6	9	15	5.92	5.45	5.64	15	0	0	0.0
11438	8	7	15	5.67	5.19	5.44	17	2	1	11.8
11439	3	10	13	5.68	5.21	5.32	14	1	1	7.1
11440	7	0	7	5.87	-----	5.87	7	0	0	0.0
11441	9	6	15	5.71	5.28	5.54	15	0	0	0.0
11442	8	6	14	5.11	5.01	5.07	14	0	0	0.0
11443	5	9	14	4.83	4.59	4.68	16	2	1	12.5
11444	10	8	18	5.70	5.44	5.58	20	2	1	10.0
11445	8	7	15	5.86	5.54	5.71	15	0	0	0.0
11446	8	5	13	5.62	5.14	5.44	13	0	0	0.0
11447	4	8	12	5.55	5.33	5.40	14	2	1	14.3
11448	NOT PREGNANT									
11449	5	9	14	6.02	5.42	5.64	14	0	0	0.0
11450	6	6	12	5.77	5.43	5.60	14	2	1	14.3

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 18 (PAGE 3): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

RAT #	DOSE GROUP III			MIDDLE DOSE			500 MG/KG/DAY		
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
NUMBER OF LIVE FETUSES									
11451	2	10	12	5.40	5.15	5.19	12	0	0.0
11452	7	6	13	5.71	5.33	5.58	14	1	7.1
11453	11	8	19	5.77	5.49	5.65	19	0	0.0
11454	10	7	17	6.02	6.18	6.08	17	0	0.0
11455	5	8	13	6.08	5.91	5.98	14	1	7.1
11456	5	8	13	5.62	5.43	5.50	14	1	7.1
11457	8	9	17	5.27	4.16	5.00	17	0	0.0
11458	12	5	17	5.21	4.94	5.13	17	0	0.0
11459	7	6	13	5.57	5.21	5.40	14	1	7.1
11460	NOT PREGNANT								
11461	7	8	15	5.96	5.60	5.77	16	1	6.2
11462	8	5	13	5.96	5.94	5.95	14	1	7.1
11463	7	9	16	5.99	5.59	5.76	17	1	5.9
11464	8	6	14	5.74	5.49	5.63	14	0	0.0
11465	9	6	15	5.87	5.73	5.81	15	0	0.0
11466	7	9	16	5.57	5.53	5.55	16	0	0.0
11467	7	7	14	6.09	5.68	5.88	15	1	6.7
11468	9	3	12	6.08	5.72	5.99	14	2	14.3
11469	7	8	15	5.32	5.27	5.29	16	1	6.2
11470	6	10	16	5.70	5.39	5.51	16	0	0.0
11471	7	6	13	5.31	4.94	5.14	14	1	7.1
11472	7	4	11	5.78	5.18	5.67	12	1	8.3
11473	7	10	17	5.36	4.85	5.06	17	0	0.0
11474	8	6	14	5.48	5.19	5.36	14	0	0.0
11475	8	7	15	5.53	5.32	5.43	16	1	6.2

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMIRCETOL IN RATS

TABLE 18 (PAGE 4): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

RAT #	DOSE	GROUP IV	NUMBER OF LIVE FETUSES			HIGH DOSE			1000 MG/KG/DAY		
			MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	TOTAL	CONCEPTUSES	RESORBED
11476			11	5	16	5.18	5.02	5.13	17	1	5.9
11477			8	6	14	5.74	5.24	5.53	14	0	0.0
11478			9	6	15	5.84	5.45	5.68	15	0	0.0
11479			7	6	13	5.59	5.27	5.44	13	0	0.0
11480			9	9	18	5.13	5.15	5.14	18	0	0.0
11481			3	9	12	5.74	5.56	5.61	13	1	7.7
11482			5	8	13	6.20	5.67	5.88	14	1	7.1
11483			13	3	16	5.08	4.81	5.03	17	1	5.9
11484			8	3	11	6.06	5.75	5.98	11	0	0.0
11485			5	9	14	5.72	5.36	5.48	14	0	0.0
11486			14	3	17	5.12	4.98	5.10	17	0	0.0
11487			10	6	16	5.61	5.42	5.54	16	0	0.0
11488			7	6	13	4.70	4.38	4.55	14	1	7.1
11489			4	8	12	4.99	4.96	4.97	12	0	0.0
11490			8	8	16	5.40	5.09	5.24	16	0	0.0
11491			6	11	17	5.57	5.22	5.35	17	0	0.0
11492			8	6	14	5.77	5.64	5.72	14	0	0.0
11493			5	11	16	5.14	4.94	5.00	16	0	0.0
11494			7	7	14	5.29	5.03	5.16	14	0	0.0
11495			8	6	14	5.36	4.80	5.12	14	0	0.0
11496			11	5	16	5.09	4.89	5.03	16	0	0.0
11497			10	7	17	5.63	5.38	5.53	17	0	0.0
11498			2	5	7	5.50	4.92	5.08	13	6	46.2
11499			9	4	13	5.73	5.28	5.59	14	1	7.1
11500			5	9	14	5.07	5.42	5.30	14	0	0.0

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DINYRCTOL IN RATS

TABLE 19 (PAGE 1): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

RAT #	CLS	VEHICLE CONTROL																				O (Vehicle) MG/KG/DAY	
		FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
11401	5/10	FA	MA	MA	FA	MA	/	FA	E	FA	FA	FA	MA	E	MA	MA	MA	MA	FA	MA	MA	MA	
11402	5/ 2	FA	5.48	5.91	5.89	5.50	5.86	5.29			5.39	5.50	5.00	5.60									5.69 5.67
11403	6/12	FA	5.56	5.90	5.51	5.96	5.40	6.10	5.92														
11404	5/10	FA	5.35	5.57	5.48	5.36	5.59	5.68	5.50	5.66	5.68	5.50	5.66	5.39	5.22	5.43	5.14	5.19	5.05	5.91	5.76	5.72	
11405	10/ 8	FA	5.89	6.04	5.24		6.01	5.38	5.33	6.02	5.42	5.77	5.50	5.48	4.86	5.41	6.06						
11406	6/ 8	FA	5.00	5.50	4.93	5.67	4.79	4.94	5.72	0.82	5.01	5.42	5.35	5.46	5.28	5.06	5.18	5.66					
11407	10/ 8	FA	5.45	5.87	5.27	6.20	6.03	5.83	5.03	5.65	5.89	5.70	5.64	5.30	5.60	5.38							
11408	3/ 9	FA	5.06		5.23	5.81	5.52	5.46	5.07	5.49	5.57	5.53	5.27	5.58	5.63	5.36	5.07	5.28					
11409																							
11410	8/ 8	MA	5.42	5.72	FA	E	MA	FA	MA	/	FA	FA	MA	FA	FA	MA	FA	MA	FA	MA	FA	MA	
11411																							
11412	9/ 6	FA	MA	FA	FA	FA	FA	MA	FA	MA	FA	MA											
11413	8/ 5	MA	5.41	5.40	5.10	5.04	5.18	4.72	4.34	5.26	5.06	5.24	5.80	5.10	5.31	5.29	5.50						
			5.10	5.32	5.48	5.74	5.54		5.34	5.12	5.72	5.73	5.83	5.58									

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION "/." DENOTES POSITION OF CERVIX
 CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (g).

PROTOCOL TIE00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 19 (PAGE 2): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	CLS	VEHICLE CONTROL										0 (VEHICLE) MG/KG/DAY								
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
11414	7/ 8	FA	MA	MA	FA	FA	FA	/ FA	FA	MA	MA	FA	MA	FA	MA	FA	FA	FA	FA	FA
		5.00	5.40	5.59	5.05	5.15	4.97	4.30	4.91	5.21	5.58	5.30	5.05	5.33	5.20	5.06				
11415	11/ 4	FA	MA	MA	MA	MA	FA	FA	FA	MA	FA	/ MA	MA	FA	MA	MA	FA	MA	MA	FA
		5.69	5.81	5.85	5.75	5.75	5.77	5.67	5.14	5.30	5.77	5.61	5.38	5.80	5.99	5.72	5.52			
11416	8/ 5	FA	MA	FA	FA	MA	MA	MA	FA	MA	FA	MA / MA	FA	FA	FA	FA	FA	FA	FA	FA
		5.17	5.01	4.93	4.92	5.16	4.71	4.94	5.19	5.21	5.10	4.37	4.85	4.68						
11417	6/ 8	FA	MA	FA	MA	FA	/ FA	FA	MA	FA	MA	FA	MA	FA	FA	FA	FA	MA	FA	MA
		5.43	5.96	5.67	5.56	5.49	5.14	5.42	5.40	5.67	5.67	5.82	5.41	5.41	5.36	5.68				
11418	7/10	FA	MA	FA	FA	MA	/ FA	FA	MA	MA	MA	MA	MA	FA	MA	MA	MA	MA	MA	MA
		5.18	5.45	5.02	4.53	5.15	4.75	4.89	5.33	5.21	5.04	4.68	4.18	5.30	4.93					
11419	5/ 9	FA	FA	FA	FA	MA	/ MA	FA	MA	MA	MA	MA	MA	FA	E	MA				
		5.04	5.30	5.05	5.08	5.81	5.33	5.36	5.80	5.38	5.35	5.49	4.74							
11420	6/ 8	MA	MA	MA	FA	FA	/ FA	FA	MA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA
		5.90	5.87	5.70	5.76	5.54	5.87	5.86	5.91	5.89	5.92	5.53	5.61	5.78	5.64					
11421	6/10	FA	MA	MA	FA	MA	MA	MA	/ MA	MA	FA	E	FA	MA	FA	FA	FA	FA	FA	FA
		5.66	5.85	5.87	5.42	5.84	5.70	5.10	5.61	5.55	5.67	5.49	6.05	5.46	5.35	6.03				
11422	9/ 3	MA	FA	FA	FA	MA	FA	MA	FA	E	MA	MA	MA							
		5.85	5.65	5.63	5.41	6.63	5.43	6.26	5.79	6.11	6.47	6.00								
11423	7/ 7	FA	FA	MA	FA	FA	/ FA	FA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	MA
		5.19	5.00	5.13	6.01	5.17	5.50	5.09	3.76	5.38	5.08	5.22	5.36	5.48	4.69					
11424	NOT PREGNANT																			
11425	9/ 7	FA	MA	FA	MA	MA	FA	/ MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	MA
		5.46	6.04	6.07	5.65	5.70	5.78	5.66	5.62	6.00	5.86	6.11	5.99	5.85						

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION "/*" DENOTES POSITION OF CERVIX
 CLS = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (g).

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS
 TABLE 19 (PAGE 3): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

RAT #	CLS	DOSAGE GROUP II										LOW DOSAGE										250 MG/KG/DAY									
		FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20									
11426	9/ 7	FA	E	MA	FA	FA	FA	MA	FA / MA	MA	FA / MA	MA	FA	FA	MA	FA	FA	MA	FA	FA	MA										
11427	3/ 6	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	FA	FA	FA	FA	FA	MA	FA	MA	FA	MA									
11428	10/ 5	FA	MA	E	MA	FA	MA	MA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA	E									
11429	9/ 4	MA	MA	MA	FA	MA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA									
11430	7/ 6	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	MA / MA	MA / MA	MA / MA	MA / MA	MA / MA	MA / MA	MA / MA	MA / MA	MA / MA	MA / MA	FA									
11431	5/ 7	FA	FA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA									
11432	12/ 8	FA	FA	FA	FA	E	MA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA									
11433	9/ 7	MA	FA	MA	MA	MA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA									
11434	9/ 5	MA	MA	FA	E	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA									
11435	9/ 9	FA	MA	FA	FA	E	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA									
11436	6/ 8	MA	MA	FA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA									
11437	8/ 7	MA	FA	FA	FA	MA	FA	FA	MA	FA	MA	FA	MA	MA	FA	MA	MA	FA	FA	FA	FA	FA									
11438	9/ 9	FA	MA	FA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	MA	MA	MA	FA									
		5.03	5.28	4.80	5.11	5.99	5.28	5.27	5.90	5.21	5.86	5.80							5.57	5.48	5.48	5.62									

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PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 19 (PAGE 4): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

RAT #	CLS	DOSAGE GROUP II										LOW DOSAGE										
		FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
11439	11/ 6	E	FA	FA	FA	FA	FA	FA	FA	FA	FA	MA	MA / FA	FA	FA	MA	FA	FA	MA	MA	MA	
11440	5/ 4	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA / FA	FA	FA	MA	MA / FA	FA	FA	MA	MA	MA	MA
11441	7/ 8	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA / MA	FA	FA	MA	FA	FA	FA	FA	MA	MA	MA
		5.50	5.64	5.60	5.86	5.70	5.18	5.56	5.32	4.86	5.21	4.83	5.72	5.81	5.26	5.33	5.52					
11442	12/ 4	FA	MA	FA	MA	MA	MA	FA	MA	MA	MA	MA / FA	MA	MA	FA	MA	FA	FA	FA	FA	FA	FA
11443	11/ 6	FA	FA	FA	FA	FA	FA	FA	FA	MA	MA	E	FA	MA / FA	MA	FA	MA	FA	MA	FA	MA	FA
		4.99	5.07	4.98	5.02	4.90	4.75	4.98	5.04	5.18	5.21	5.05	5.47	5.24	5.06							
11444	11/ 9	FA	MA	MA	MA	MA	MA	FA	MA	FA	MA	FA / MA	FA	FA	MA	FA	MA	FA	MA	FA	MA	MA
		5.08	5.08	5.28	6.01	5.66	5.63	5.51	5.51	5.87	5.24	5.24	4.43	4.59	5.04	4.35	5.21	4.33	4.68	4.73		
11445	7/ 8	MA	FA	FA	MA	MA	FA	MA	FA	MA	MA	MA / FA	MA	MA	FA	MA	FA	MA	FA	MA	MA	MA
		6.15	5.52	5.11	5.40	5.66	5.88	5.80	5.81	5.43	5.43	5.95	5.30	5.69	6.15	5.63	5.85					
11446	8/ 5	FA	FA	FA	MA	MA	MA	MA	MA	FA / MA	MA	MA / FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA
		5.11	5.17	4.84	5.57	5.75	5.51	5.59	5.43	5.49	5.81	5.63	5.61	5.16								
11447	6/ 9	FA	FA	FA	MA	FA	MA	FA	MA	FA / MA	MA	MA / FA	MA	MA	FA	MA	FA	MA	FA	MA	MA	MA
		5.34	5.22	4.84	5.28	6.01	5.60	5.53	5.50	5.20	5.48	5.43	5.41									
11448	NOT PREGNANT																					
11449	5/ 9	FA	FA	FA	FA	FA	MA / FA	MA	FA	MA	MA	FA	MA	FA	FA	MA	FA	FA	MA	MA	MA	
		4.92	5.38	5.38	5.29	6.28	5.79	5.84	5.55	5.88	6.07	5.69	5.27	5.53	6.03							
11450	8/ 6	FA	MA	E	MA	MA	MA	FA / FA	MA	FA	MA	FA	FA	FA	FA	MA	FA	FA	FA	FA	FA	FA
		5.03	5.96						5.66	5.77	5.52	5.49	5.30	6.15	5.86	5.57	5.55	5.37				

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PROTOCOL TIF00007: ORAL (GRAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 19 (PAGE 5): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	CLS	MIDDLE DOSAGE																			500 MG/KG/DAY					
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20					
11451	8/ 8	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA
11452	6/ 8	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	E	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA
11453	9/10	FA	FA	MA	MA	MA	MA	MA	MA	MA	MA	FA	FA	/ MA	MA	FA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA
11454	9/ 8	FA	MA	FA	MA	FA	MA	FA	MA	MA	MA	MA	FA	MA	FA	MA	MA	FA	MA	MA	FA	MA	FA	MA	FA	FA
11455	8/ 6	FA	FA	FA	MA	FA	MA	FA	MA	MA	FA	MA	FA	/ FA	MA	FA	MA	FA	E	MA	FA	MA	FA	MA	FA	MA
11456	7/ 7	FA	MA	FA	MA	FA	MA	FA	MA	FA	FA	/ FA	FA	/ E	MA	FA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA
11457	8/11	FA	MA	FA	FA	FA	MA	MA	MA	MA	MA	MA	FA	MA	FA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	MA
11458	9/ 8	FA	MA	MA	MA	FA	MA	MA	MA	MA	MA	MA	FA	/ FA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA
11459	7/ 7	MA	MA	MA	FA	E	FA	MA	FA	FA	FA	MA	FA	MA	FA	MA	MA	FA	MA	MA	FA	MA	MA	FA	MA	FA
11460	NOT PREGNANT																									
11461	7/10	FA	MA	E	FA	MA	FA	MA	/ MA	FA	FA	FA	FA	FA	FA	MA	FA	MA	MA	FA	MA	FA	MA	FA	MA	FA
11462	6/ 8	FA	E	FA	MA	MA	/ MA	MA	MA	FA	MA	MA	FA	MA	MA	FA	MA	MA	FA	MA	MA	FA	MA	MA	FA	MA
11463	11/ 7	MA	FA	MA	MA	E	FA	MA	MA	FA	FA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION "/> DENOTES POSITION OF CERVIX
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PROTOCOL TIE00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRGETOL IN RATS

TABLE 19 (PAGE 6): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

		DOSE GROUP III										MIDDLE DOSAGE									500 MG/KG/DAY								
		FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20							
RAT #	CLS																												
11464	6/ 9	FA	MA	MA	FA	FA / MA	MA	FA	MA	MA	FA	MA	MA	FA	MA	MA	FA	MA	MA	FA									
11465	11/ 5	FA	FA	MA	MA	MA	MA	MA	MA	MA	FA / FA	MA	MA	FA	MA	MA	FA	MA	MA	FA									
11466	10/ 7	MA	MA	MA	MA	FA	FA	FA	FA	FA	FA / FA	FA	FA	FA	FA	MA	MA	FA	MA	MA									
11467	7/10	MA	E	FA	FA	FA	FA	MA / MA	FA	MA	MA / MA	FA	MA	MA	FA	MA	MA	FA	FA	FA									
11468	6/ 9	FA	MA	MA	MA	MA	MA	MA	MA	MA / E	MA / E	MA	FA	E	MA	MA	MA	FA	MA	FA									
11469	10/ 6	E	FA	FA	FA	FA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA	MA	FA	FA									
11470	9/10	FA	MA	FA	FA	MA	FA	FA	FA	MA / MA	FA	MA	FA	MA	MA	FA	FA	MA	FA	FA									
11471	14/ 6	E	MA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	MA	MA	MA	MA									
11472	8/ 4	FA	FA	MA	MA	MA	MA	E	FA	MA	MA	MA	MA	MA	FA	MA	FA	MA	FA	FA									
11473	12/10	FA	MA	FA	MA	MA	FA	MA	FA	MA	FA / FA	MA	FA	FA	MA	MA	FA	FA	MA	FA									
11474	7/ 7	MA	MA	MA	FA	MA	MA	MA	FA	MA	MA / FA	FA	FA	FA	MA	MA	MA	MA	MA	MA									
11475	10/ 6	FA	FA	MA	E	MA	MA	MA	MA	MA	FA / FA	FA	FA	FA	MA	MA	MA	MA	MA	FA									

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION "/" DENOTES POSITION OF CERVIX
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PROTOCOL TIF00007: ORAL (Gavage) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 19 (PAGE 7): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

RAT #	CLS	DOSAGE GROUP IV										HIGH DOSAGE										1000 MG/KG/DAY									
		FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20									
11476	6/11	MA	MA	MA	E	MA	MA	MA	MA	FA	FA	MA	MA	MA	FA	FA	FA	FA	FA	FA	MA										
11477	9 / 6	FA	MA	FA	MA	FA	MA	FA	FA	MA	/	MA	FA	MA	FA	MA	FA	MA	FA	FA	MA										
11478	6/10	FA	MA	MA	MA	MA	FA	/	MA	MA	MA	FA	MA	MA	FA	MA	FA	MA	FA	MA	FA										
11479	6 / 8	FA	MA	FA	MA	FA	MA	FA	/	MA	MA	FA	MA	MA	FA	MA	FA	MA	FA	FA	FA										
11480	12 / 8	FA	MA	MA	MA	FA	FA	FA	FA	MA	MA	MA	MA	FA	/	FA	FA	FA	MA	FA	MA										
11481	8 / 6	FA	FA	FA	FA	FA	MA	FA	MA	FA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	MA										
11482	8 / 6	FA	MA	FA	MA	FA	MA	FA	E	FA	FA	/	MA	FA	FA	FA	MA	FA	FA	MA	FA	MA									
11483	8 / 9	FA	MA	MA	MA	MA	MA	FA	MA	MA	MA	MA	MA	FA	MA																
11484	4 / 7	MA	MA	MA	MA	MA	FA	MA	MA	FA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	MA										
11445	8 / 6	MA	MA	MA	FA	MA	FA	FA	FA	/	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA										
11486	8 / 9	MA	MA	MA	MA	FA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA										
11487	6/10	MA	FA	MA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	MA	MA	MA	MA	MA	FA										
11488	10 / 7	MA	FA	MA	MA	FA	FA	FA	FA	MA	FA	FA	MA	FA	MA	E	MA	FA	MA	FA	MA										

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION "/" DENOTES POSITION OF CERVIX
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PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRGETOL IN RATS

TABLE 19 (PAGE 8): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

RAT #	CLS	DOSE GROUP IV										HIGH DOSAGE										1000 MG/KG/DAY									
		FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20									
11489	6/ 8	MA	FA	FA	FA	FA / FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA		
11490	9/ 7	MA	FA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA / FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	FA	
11491	12/ 5	FA	MA	FA	MA	MA	MA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	
11492	7/ 8	FA	FA	FA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA / FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA	FA	
11493	15/ 8	FA	MA	FA	MA	MA	FA	MA	FA	MA	FA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA		
11494	6/ 8	MA	FA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	
11495	8/ 8	MA	FA	MA	MA	MA	MA	FA	MA	FA	FA	FA	FA	FA	FA	MA	MA	FA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	
11496	9/ 7	MA	MA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	
11497	11/ 7	MA	FA	FA	MA	FA	MA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	
11498	4/11	E	E	MA	/ FA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	E	FA	FA	E	E	E	E	E	E	E	E	E	E	E	E	
11499	9/ 5	MA	MA	FA	MA	FA	MA	MA	MA	MA	MA	MA	FA	FA	E / MA	MA	FA	MA	FA	MA	FA	MA	MA	MA	MA	MA	MA	MA	MA	MA	
11500	8/ 8	FA	FA	MA	FA	MA	FA	MA	FA	MA	FA	MA	FA	FA	FA	MA	MA	FA	MA	FA	MA	FA	MA	FA							

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION "/" DENOTES POSITION OF CERVIX
 CLS = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL T1F00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 20 (PAGE 1): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSEAGE GROUP I		VEHICLE CONTROL		0 (VEHICLE) MG/KG/DAY	
SPECIMENS WITH ANY ALTERATIONS	N/N	GROSS EXTERNAL EXAMINATION	SOFT TISSUE EXAMINATION	SKELETAL EXAMINATION	N/N
RAT NUMBER	ALTERATIONS N/N (%)	DESCRIPTION	DESCRIPTION	DESCRIPTION	DESCRIPTION
11401	1 (8.3)	1/12	FETUS 8 BODY: GASTROSCHISIS, portion of small intestine protrudes through abdominal area	1/ 6 FETUS 8 INTESTINES: PORTION OF INTESTINE PROTRUDING THROUGH UMBILICUS	0/ 6
11402	0 (0.0)	0/ 7		0/ 3	0/ 4
11403	0 (0.0)	0/17		0/ 8	0/ 9
11404	0 (0.0)	0/14		0/ 6	0/ 8
11405	2 (13.3)	0/15	FETUS 8 LATE RESORPTION, autolysis precludes evaluation	0/ 7	2/ 8 FETUS 5 THORACIC VERTEBRAE: CENTRUM, BIFID, 11th
				FETUS 16 RIBS: SHORT, right 13th	
11406	0 (0.0)	0/14		0/ 7	0/ 7
11407	0 (0.0)	0/15		0/ 7	0/ 8
11408	0 (0.0)	0/10		0/ 5	0/ 5
11409	NOT PREGNANT				
11410	1 (7.1)	0/14		0/ 7	1/ 7 FETUS 4 THORACIC VERTEBRAE: CENTRUM, BIFID, 11th
11411	NOT PREGNANT				

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 20 (PAGE 2): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP I	GROSS EXTERNAL EXAMINATION			SOFT TISSUE EXAMINATION			SKELETAL EXAMINATION
	RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N (N)	N/N	DESCRIPTION	N/N	DESCRIPTION	
11412	3 (20.0)	0/15			0 / 7		3 / 8 FETUS 3 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right
							FETUS 7 RIBS: SHORT, left 13th
							FETUS 13 RIBS: SHORT, right 13th
11413	1 (9.1)	0/11			0 / 5		1 / 6 FETUS 1 THORACIC VERTEBRAE: CENTROM, BIFID, 10th
11414	1 (6.7)	0/15			1 / 7 FETUS 10 VESSELS: INNOMINATE ARTERY ABSENT		0 / 8
11415	0 (0.0)	0/15			0 / 7		0 / 8
11416	0 (0.0)	0/13			0 / 6		0 / 7
11417	2 (14.3)	0/14			0 / 7		2 / 7 FETUS 5 RIBS: WAVY, right 6th - 7th, 10th and 11th; left 5th - 7th and 11th
11418	0 (0.0)	0/14			0 / 7		0 / 7

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TTF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 20 (PAGE 3): FETAL ALTERATIONS - INDIVIDUAL DATA

SPECIMENS WITH ANY ALTERATIONS	N/N	DESCRIPTION	0 (VEHICLE) MG/KG/DAY	
			VEHICLE CONTROL	SOFT TISSUE EXAMINATION
DOSAGE GROUP I				
11419	0 (0.0)	0/13	0 / 6	0 / 7
11420	0 (0.0)	0/14	0 / 7	0 / 7
11421	0 (0.0)	0/15	0 / 7	0 / 8
11422	1 (9.1)	0/11	0 / 5	1 / 6
				FETUS 10 THORACIC VERTEBRAE: CENTRUM, BIFID, 10th
11423	0 (0.0)	0/14	0 / 7	0 / 7
11424	NOT PREGNANT			
11425	0 (0.0)	0/13	0 / 6	0 / 7

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 20 (PAGE 4): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP II		LOW DOSAGE		250 MG/KG/DAY	
RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N (%)	GROSS EXTERNAL EXAMINATION	SOFT TISSUE EXAMINATION	SKELETAL EXAMINATION	N/N
11426	1 (8.3)	0/12	1/ 6	FETUS 13 VESSELS: UMBILICAL ARTERY DESCENDS TO LEFT OF URINARY BLADDER	0/ 6
11427	0 (0.0)	0/ 9	0/ 4		0/ 5
11428	0 (0.0)	0/13	0/ 6		0/ 7
11429	0 (0.0)	0/11	0/ 4		0/ 7
11430	0 (0.0)	0/13	0/ 6		0/ 7
11431	0 (0.0)	0/12	0/ 5		0/ 7
11432	0 (0.0)	0/14	0/ 7		0/ 7
11433	0 (0.0)	0/ 9	0/ 4		0/ 5
11434	0 (0.0)	0/11	0/ 5		0/ 6
11435	0 (0.0)	0/16	0/ 8		0/ 8
11436	0 (0.0)	0/14	0/ 7		0/ 7
11437	0 (0.0)	0/15	0/ 7		0/ 8
11438	2 (13.3)	0/15	1/ 7	FETUS 16 VESSELS: UMBILICAL ARTERY DESCENDS TO LEFT OF URINARY BLADDER	1/ 8
11439	0 (0.0)	0/13	0/ 6		0/ 7
11440	0 (0.0)	0/ 7	0/ 3		0/ 4

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 20 (PAGE 5): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSE GROUP II	LOW DOSAGE			250 MG/KG/DAY		
	RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N/N (%)	GROSS EXTERNAL EXAMINATION	SOFT TISSUE EXAMINATION	SKELETAL EXAMINATION	
11441	0 (0.0)	0/15		0/ 7		0/ 8
11442	0 (0.0)	0/14		0/ 7		0/ 7
11443	3 (21.4)	0/14		0/ 7	FETUS 1 CERVICAL VERTEBRAE; CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, left	3/ 7
					FETUS 3 CERVICAL VERTEBRAE; CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right	
					FETUS 9 CERVICAL VERTEBRAE; CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right	
11444	0 (0.0)	0/18		0/ 9		0/ 9
11445	0 (0.0)	0/15		0/ 7		0/ 8
11446	0 (0.0)	0/13		0/ 6		0/ 7
11447	1 (8.3)	0/12		0/ 6	FETUS 9 THORACIC VERTEBRAE; CENTRUM, BIFID, 13th	1/ 6
11448	NOT PREGNANT					

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 20 (PAGE 6): FETAL ALTERATIONS - INDIVIDUAL DATA

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS	GROSS EXTERNAL EXAMINATION		SOFT TISSUE EXAMINATION		SKELETAL EXAMINATION	
		N/N	DESCRIPTION	N/N	DESCRIPTION	N/N	DESCRIPTION
11449	0 (0.0)	0/14		0 / 7		0 / 7	
11450	1 (8.3)	0/12		0 / 6		1 / 6	FETUS 1 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, bilateral

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 20 (PAGE 7): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP III	GROSS EXTERNAL EXAMINATION			SOFT TISSUE EXAMINATION			SKELETAL EXAMINATION		
	RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N (%)	N/N	DESCRIPTION	N/N	DESCRIPTION	N/N	DESCRIPTION	N/N
11451	1 (8.3)		0/12		1/ 6	FETUS 10 VESSELS: UMBILICAL ARTERY DESCENDS TO LEFT OF URINARY BLADDER	0/ 6		
11452	0 (0.0)		0/13		0/ 6		0/ 7		
11453	1 (5.3)		0/19		1/ 9	FETUS 2 VESSELS: UMBILICAL ARTERY DESCENDS TO LEFT OF URINARY BLADDER	0/10		
11454	0 (0.0)		0/17		0/ 8		0/ 9		
11455	0 (0.0)		0/13		0/ 6		0/ 7		
11456	1 (7.7)		0/13		0/ 6		1/ 7	FETUS 10 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, left	
11457	0 (0.0)		0/17		0/ 8		0/ 9		
11458	0 (0.0)		0/17		0/ 8		0/ 9		
11459	0 (0.0)		0/13		0/ 6		0/ 7		
11460	NOT PREGNANT								
11461	0 (0.0)		0/15		0/ 7		0/ 8		
11462	0 (0.0)		0/13		0/ 6		0/ 7		
11463	0 (0.0)		0/16		0/ 8		0/ 8		
11464	0 (0.0)		0/14		0/ 7		0/ 7		

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 20 (PAGE 8): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP III	SPECIMENS WITH ANY ALTERATIONS			GROSS EXTERNAL EXAMINATION			MIDDLE DOSAGE			SOFT TISSUE EXAMINATION			500 MG/KG/DAY			SKELETAL EXAMINATION		
	RAT NUMBER	N	%	N/N	DESCRIPTION	N/N	DESCRIPTION	N/N	DESCRIPTION	N/N	DESCRIPTION	N/N	DESCRIPTION	N/N	DESCRIPTION	N/N	DESCRIPTION	
11465	0	(0.0)		0/15		0/ 7		0/ 8		0/ 8		0/ 8		0/ 8		0/ 8		
11466	0	(0.0)		0/16		0/ 8		0/ 8		0/ 8		0/ 8		0/ 8		0/ 8		
11467	1	(7.1)		0/14		0/ 7		1/ 7	FETUS 14 STERNAL CENTRA: FUSED, 2nd - 4th; ASYMMETRIC, 2nd and 3rd		1/ 7							
11468	0	(0.0)		0/12		0/ 6		0/ 6		0/ 6		0/ 6		0/ 6		0/ 6		
11469	0	(0.0)		0/15		0/ 7		0/ 8		0/ 8		0/ 8		0/ 8		0/ 8		
11470	0	(0.0)		0/16		0/ 8		0/ 8		0/ 8		0/ 8		0/ 8		0/ 8		
11471	0	(0.0)		0/13		0/ 6		0/ 7		0/ 7		0/ 7		0/ 7		0/ 7		
11472	0	(0.0)		0/11		0/ 5		0/ 6		0/ 6		0/ 6		0/ 6		0/ 6		
11473	0	(0.0)		0/17		0/ 8		0/ 9		0/ 9		0/ 9		0/ 9		0/ 9		
11474	1	(7.1)		0/14		1/ 7	FETUS 8 VESSELS; UMBILICAL ARTERY DESCENDS TO LEFT OF URINARY BLADDER	0/ 7		0/ 7	FETUS 8 VESSELS; UMBILICAL ARTERY DESCENDS TO LEFT OF URINARY BLADDER	0/ 7		0/ 7	FETUS 11 VESSELS; UMBILICAL ARTERY DESCENDS TO LEFT OF URINARY BLADDER	0/ 7		
11475	1	(6.7)		0/15		1/ 7		0/ 8		0/ 8		0/ 8		0/ 8		0/ 8		

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TIF00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 20 (PAGE 9): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSE GROUP IV		HIGH DOSAGE		1000 MG/KG/DAY		SKELETAL EXAMINATION	
RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N/N (%)	GROSS EXTERNAL EXAMINATION	SOFT TISSUE EXAMINATION	N/N	DESCRIPTION	N/N	DESCRIPTION
11476	1 (6.2)	0/16	0/ 8	1/ 8	FETUS 4 STERNAL CENTRA; INCOMPLETELY OSSIFIED, 1st	1/ 8	FETUS 4 STERNAL CENTRA;
11477	0 (0.0)	0/14	0/ 7	0/ 7		0/ 7	
11478	0 (0.0)	0/15	0/ 7	0/ 8		0/ 8	
11479	0 (0.0)	0/13	0/ 6	0/ 7		0/ 7	
11480	1 (5.6)	0/18	0/ 9	1/ 9	FETUS 15 THORACIC VERTEBRAE; CENTRUM, BIFID, 5th	1/ 9	THORACIC VERTEBRAE; CENTRUM, BIFID, 5th
11481	0 (0.0)	0/12	0/ 6	0/ 6		0/ 6	
11482	1 (7.7)	0/13	1/ 6	FETUS 9 KIDNEYS: PELVIS, SLIGHT DILATION, right	0/ 7	0/ 7	
11483	1 (6.2)	0/16	1/ 8	FETUS 12 KIDNEYS: PELVIS, SLIGHT DILATION, bilateral	0/ 8	0/ 8	
11484	1 (9.1)	0/11	0/ 5	1/ 6	FETUS 7 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right	1/ 6	CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right
11485	0 (0.0)	0/14	0/ 7	0/ 7		0/ 7	
11486	0 (0.0)	0/17	0/ 8	0/ 9		0/ 9	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TIE00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYRCETOL IN RATS

TABLE 20 (PAGE 10): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP IV	HIGH DOSAGE			1000 MG/KG/DAY		
	SPECIMENS WITH ANY ALTERATIONS	GROSS EXTERNAL EXAMINATION	SOFT TISSUE EXAMINATION	SKELETAL EXAMINATION		
RAT NUMBER	N/N	DESCRIPTION	N/N	DESCRIPTION	N/N	DESCRIPTION
11487	0 (0.0)	0/16	0 / 8		0 / 8	
11488	3 (23.1)	0/13	1 / 6	FETUS 4 EYES: RETINA FOLDED, left	2 / 7	FETUS 5 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, left
						FETUS 9
						CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, bilateral
11489	1 (8.3)	0/12	0 / 6		1 / 6	FETUS 5 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right
11490	0 (0.0)	0/16	0 / 8		0 / 8	
11491	0 (0.0)	0/17	0 / 8		0 / 9	
11492	1 (7.1)	0/14	0 / 7		1 / 7	FETUS 11 THORACIC VERTEBRAE: CENTRUM, BIFID, 11th

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL TIE00007: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF DIMYCETOL IN RATS

TABLE 20 (PAGE 11): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP IV	HIGH DOSAGE			1000 MG/KG/DAY		
	SPECIMENS WITH ANY ALTERATIONS	GROSS EXTERNAL EXAMINATION	SOFT TISSUE EXAMINATION	SKELETAL EXAMINATION		
RAT NUMBER	N/N	DESCRIPTION	N/N	DESCRIPTION	N/N	DESCRIPTION
11493	2 (12.5)	1/16 FETUS 9 TAIL: THREAD-LIKE	0/ 8		2 / 8	FETUS 9 SACRAL VERTEBRAE: 2 PRESENT a; CAUDAL VERTEBRAE: 0 PRESENT a
11494	1 (7.1)	0/14				FETUS 15 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right
			1 / 7	FETUS 10 VESSELS: UMBILICAL ARTERY DESCENDS TO LEFT OF URINARY BLADDER	0 / 7	
11495	0 (0 . 0)	0/14	0 / 7		0 / 7	
11496	0 (0 . 0)	0/16	0 / 8		0 / 8	
11497	0 (0 . 0)	0/17	0 / 8		0 / 9	
11498	0 (0 . 0)	0 / 7	0 / 3		0 / 4	
11499	1 (7.7)	0/13	0 / 6		1 / 7	FETUS 1 STERNAL CENTRA: INCOMPLETELY OSSIFIED, 1st
11500	1 (7.1)	0/14	0 / 7		1 / 7	FETUS 5 LUMBAR VERTEBRAE: CENTRUM, UNILATERAL OSSIFICATION, right 1st

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

a. Excluded from ossification site summarization and statistical analyses.